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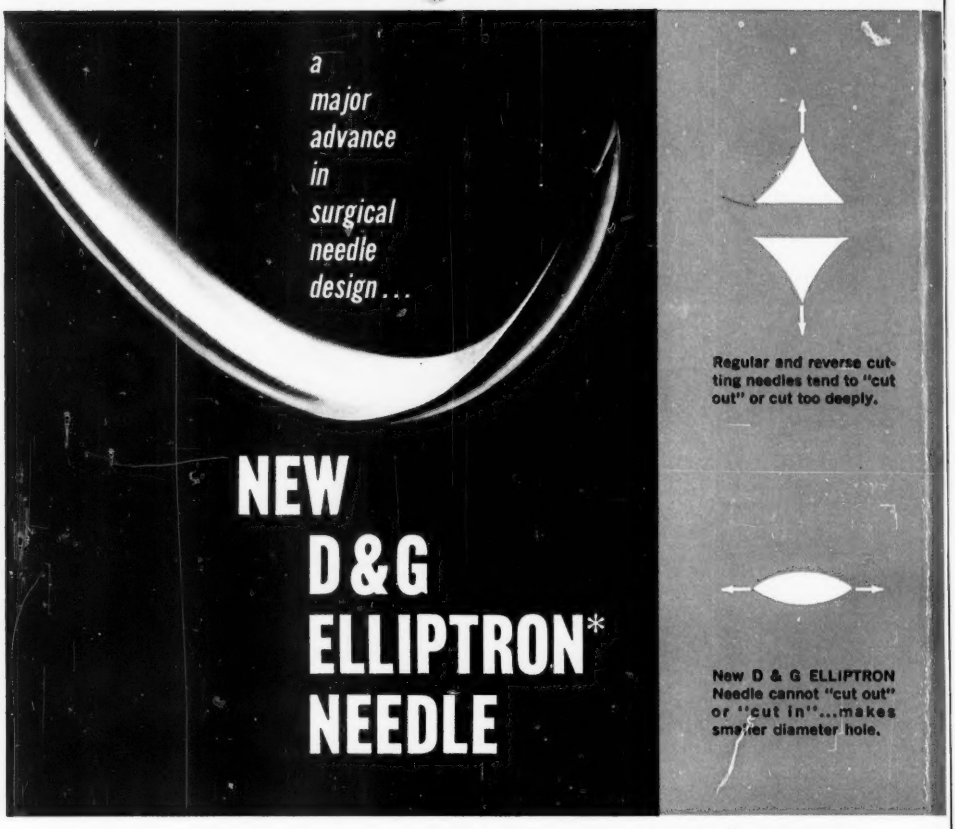

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BACTERIOLOGIC AND CLINICAL EXPERIENCES AND THE METHODS OF CONTROL OF HOSPITAL INFECTIONS DUE TO ANTIBIOTIC RESISTANT STAPHYLOCOCCI

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IN THE EARLY DAYS of the antibiotic era when it appeared that the problem of infectious disease had been forever solved, an occasional voice was heard predicting the possibility that as a result of the use of these antibiotics a new breed of organism would result which would be resistant to the so-called wonder drugs. This prediction has proved to be correct for both gram-positive and gram-negative organisms.

At the present time, the most significant problem with antibiotic resistant organisms is that of the antibiotic resistant Micrococcus pyogenes var. aureus (hereafter referred to as Staphylococcus aureus). Increasing numbers of reports of these organisms as the cause of hospital infections are appearing in the literature both in this country and abroad. Infections with these organisms do not constitute a serious problem in the general population. They do, however, present a serious problem in hospitalized patients. There is no doubt that many of our modern institutions are infested with them. They have been reported as being the source of infections in clean surgical wounds, in newborn nurseries as cutaneous infections, in postpartum nursing mothers as breast abscesses, in the respiratory tract as staphylococcic pneumonia, in severe types of enteritis in postoperative surgical patients, and in cutaneous infections involving nonsurgical hospital patients and hospital personnel. As Howe has stated, the true extent of this problem is not known but it is certainly far more widespread than can be ascertained from the literature. Conversation and communication with physicians from widely scattered institutions in this country have revealed hospital infections with these organisms to be nationwide. Institutions which do not perform routine

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TABLE I.—PATIENTS WITH INFECTIONS CAUSED BY COAGULASE POSITIVE STAPHYLOCOCCUS AUREUS, FEBRUARY 1956 TO JANUARY 1957

	Phage type 42B-52-81		*Other phage type or negative phage*		
	No.	*Per cent*	*No.*	*Per cent*	*Total*
Clean surgical wounds	66	48	70	52	136
Infected traumatic wounds and burns	15	53	13	47	28
Staphylococcic pneumonia	5	62	3	38	8
Staphylococcic cutaneous infections in hospital patients not related to surgery	44	76	14	24	58
Patients admitted with staphylococcic infections unrelated to hospitalization	14	16	73	84	87

bacteriologic studies, including antibiotic susceptibility tests, on all infections and which do not closely evaluate infection rates may not be conscious of the prevalence of these organisms.

Early in 1956, we became interested in staphylococcal infections occurring in hospitalized patients. This report concerns our findings for a 1 year period.

METHODS AND MATERIALS

Culture methods. Specimens from patients were routinely inoculated onto the surface of two blood agar plates (2 per cent trypticase soy with 8 per cent defibrinated horse blood). Both plates were incubated overnight at 37 degrees C., one plate aerobically and the other anaerobically.

Nasal specimens from the hospital personnel were obtained with sterile, cotton-tipped swabs moistened in sterile saline. The swabs were inserted about ½ inch into each nostril and immediately inoculated to a blood agar plate. Following overnight aerobic incubation at 37 degrees C., all colonies on the plate were identified. No culture media were employed in this study which were selective of staphylococcus or inhibitive of other organisms.

Nasal specimens from preoperative patients were obtained just before anesthesia was induced. Sterile cotton-tipped swabs moistened with sterile 3 per cent trypticase soy broth were used. Each swab was delivered to the laboratory in a small tube of trypticase soy broth. Inoculation was then made to a blood agar plate.

Numerous hospital articles were also cultured. These included blankets, linens, soaps, lubricating jellies, surgical instruments, suture materials, bone wax, irrigating fluid, anesthesia masks, airways, and intubation tubes. Occasional spot check cultures were made of surgeons' hands before and after scrubbing and after various periods of operating.

Coagulase test. This test was performed on all isolated staphylococci regardless of pigment or hemolysis production. Human plasma diluted 1:3 with isotonic saline or desiccated coagulase plasma reconstituted with 5 milliliters of saline per ampule was used. Three colonies of staphylococci were picked from the surface of the blood agar plate and inoculated to a tube containing 0.2 cubic centimeter of plasma. The coagulase test was read following overnight incubation at 37 degree C. This report is concerned only with coagulase positive staphylococci isolated from personnel carriers or from patients with an actual infection.

Bacteriophage typing of staphylococci. As Blair has emphasized, any study of a staphylococcus problem is of limited value unless bacteriophage typing of the organism is carried out. The bacteriophages supplied by Blair and used for typing the coagulase positive staphylococci were as follows:

3A	3B	3C	6	7
29	39	42B	42D	42E
44A	47	52	52A	53
54	55	70	73	75
77	79	81	523	VA4

The method of Blair and Carr (as modified by them) was employed in the propagation of the bacteriophage and the typing of the staphylococci.

Antibiotic resistance determination. Test tube susceptibility tests were performed. All antibiotics were reconstituted from the dried form with 3 per cent trypticase soy broth except neomycin and polymyxin which were dissolved in tryptose phosphate broth as recommended by Waisbren. Three stock

solutions of each antibiotic were made up in concentrations of 2, 20, and 200 units or micrograms per milliliter. To 0.5 cubic centimeter of each of the stock solutions was added 0.5 cubic centimeter of a 1:1000 dilution (in trypticase soy broth except for neomycin and polymyxin) of an overnight broth culture. Therefore, the final concentration in each test was 1, 10, and 100 units or micrograms of antibiotic per milliliter. The tests were incubated for 24 hours at 37 degrees C. and susceptibility determined by lack of turbidity in the tube.

RESULTS

Early in our study, it became apparent that the staphylococcus causing our severe infections was a strain lysed by 3 of the bacteriophages, i.e., 42B, 52, and 81. It should be noted that this bacteriophage type 42B/52/81 accounted for approximately 50 per cent of all postoperative wound infections and pneumonias (Table I). This same organism was responsible for 76 per cent of the cutaneous abscesses acquired by patients during hospitalization but not related to surgery, and also accounted for 80 per cent of the typed organisms from the cutaneous infections in hospital personnel (Table II). While firmly entrenched in the hospital, 42B/52/81 was not solely limited to our institution, inasmuch as 16 per cent of the patients admitted to this hospital with established staphylococcic infection were infected with this same phage type organism.

When antibiotic susceptibilities of the staphylococci from 158 patients were studied by the test tube method (Fig. 1), it was found that the bacteriophage type 42B/52/81 had an extremely high percentage of resistance to 10 units or micrograms per milliliter of penicillin, streptomycin, tetracycline, and erythromycin. The staphylococci not lysed by any of the bacteriophages (designated negative) approached this high degree of resistance, while the organisms lysed by bacteriophages other than 42B, 52, and 81 were less resistant to these 4 antibiotics. Of these 158 staphylococci, only 1 was found resistant to 10 micrograms per milliliter of novobiocin, 1 to neomycin, and about 50 per cent to magnamycin. All were susceptible to bacitracin and chloramphenicol.

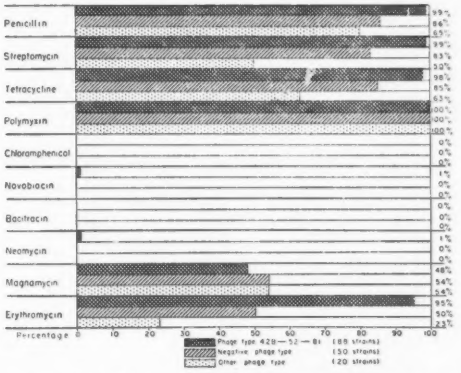

FIG. 1. Antibiotic resistance to 10 units or micrograms per milliliter (158 strains isolated from patient infections).

Nasal carriers in hospital personnel. Six hundred and forty members of the hospital personnel were surveyed with nasal cultures and 265 (41 per cent) of these were found to be carriers of a coagulase positive Staphylococcus aureus. Bacteriophage typing of these organisms revealed that only 11 (4 per cent) were the significant phage type 42B/52/81 which was responsible for 69 per cent of hospital infections (Table III). Repeat nasal cultures on the positive carriers were not uniformly consistent with the original culture. Because of this fact, treatment with the appropriate antibiotics was not carried out. The individuals themselves were informed as to the result of the culture primarily in an effort to acquaint them with the fact that they were potentially a source of infection and that they should be meticulous in their techniques.

Antibiotic resistant staphylococcal infections in clean surgical wounds. Ten thousand open operative procedures are done each year at the Temple University medical center. Prior to February of 1956, no comprehensive record of the infections in clean surgical wounds was kept. Beginning in February

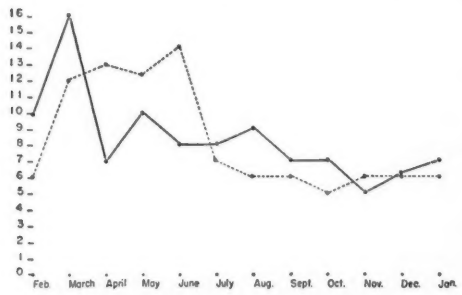

FIG. 2. Percentage frequency distribution of 323 hospital acquired patient infections, •—• and 137 personnel infections, o---o (by month).

1956, there was a marked rise in the number of clean surgical wounds showing infection, and analysis revealed an infection rate of approximately 5 per cent. Following institution of methods of control as outlined, the rate of clean surgical wound infection fell to an acceptable level of 0.8 to 1.5 per cent and has remained at that level for the past 10 months. During the course of our study for the year 1956, there were a total of 164 antibiotic resistant staphylococcal infections in surgical wounds. Approximately 50 per cent (Table I) were of phage type 42B/52/-81. As shown in Figure 1, these organisms showed a significant degree of resistance to penicillin, streptomycin, tetracycline, and erythromycin, and practically all were sensitive to novobiocin, chloramphenicol, neomycin, and bacitracin. These patients were treated by adequate opening of the wound as soon as the presence of infection was established. Cultures and susceptibility studies were done promptly. If the infection was a severe one, novobiocin or chloramphenicol was given immediately prior to obtaining the laboratory report. Otherwise, the administration of these drugs was delayed until the culture and susceptibilities were available and it was obvious that the infection was of such severity that it could not be adequately treated by surgical drainage alone. Those patients who required the use of novobiocin or chloramphenicol in the treatment of their infections showed almost uniformly excellent response to the administration of these agents. The local use of bacitracin or neomycin was occasionally employed. The response of the infected wound to these local agents was disappointing, and it is our opinion that adequate local drainage alone is equally effective in most instances. A few of these infected surgical wounds exhibited marked chronicity despite adequate drainage. The organisms responsible for these infections were resistant to all antibiotics with the exception of novobiocin, chloramphenicol, neomycin, and bacitracin. These patients were given novobiocin and in most instances prompt healing occurred. In 2 patients who were treated in this manner there was recurrence of the infection after wound closure and an additional course of novobiocin was required to obtain permanent wound healing.

TABLE II.—BACTERIOPHAGE TYPES OF STAPHYLOCOCCI FROM PATIENT AND PERSONNEL INFECTIONS AND PERSONNEL CARRIERS

	Bacteriophage type						
	42B-52-81		*Other*		*Negative*		
	No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*Total*
Hospital acquired infections in patients	205	63	44	14	74	23	323
Hospital unrelated infections in patients	14	16	25	29	48	55	87
Infections in hospital personnel	110	80	16	11	11	9	137
Personnel nasal carriers	11	4	153	58	101	38	265

The total of 323 hospital acquired infections includes breast abscesses occurring in the postpartum period and cutaneous infections in newborn infants which will be reported separately.

Cutaneous infections with antibiotic resistant staphylococci in hospital personnel. As noted in Figure 2, there was a sharp rise in cutaneous staphylococcal infections in hospital personnel concomitant with the development of these infections in hospital patients. Likewise, the infection rate in hospital personnel fell with the fall in the patient infection rate. There is no doubt that the origin of these infections in hospital personnel was through direct contact with the infected patient, and, in turn, infected personnel were capable of transmitting these cutaneous infections to other hospital patients. During the year 1956, there were 137 cutaneous infections with antibiotic resistant staphylococci

in 99 hospital personnel. It is interesting to note that 79 of the 99 personnel with infection were nurses and that 64 of these were student nurses and only 15 registered nurses (Fig. 3). The student nurse has the most intimate patient contact. In Figure 4, the site of these cutaneous infections is outlined. Sixty-four per cent of these infections involved forearm, hands, and face which are the cutaneous surfaces readily exposed to contamination while in nursing uniform.

The majority of these infections were furuncular in type. An occasional one was a true carbuncle. They were frequently multiple and the majority of personnel suffered one or more recurrences. None was seriously ill.

As soon as the infection was noted, the individuals were taken off duty. Treatment consisted initially of warm compresses and drainage when fluctuation was evident. Attempts at early drainage on several occasions resulted in a flare-up of the infection and evidences of spread. The individual was instructed to use hexachlorophene soap for bathing and 70 per cent alcohol was used liberally on the involved areas and on the hands. Those individuals with multiple lesions or recurrent lesions in localized areas such as the axilla were treated with ultraviolet light with good results. Autogenous vaccine prepared with bacteriophage type 42B/52/81 was also used in a considerable number of these personnel with recurrent lesions. The staff was divided in its impression of the value of the vaccine.

Hospital personnel with recurrent staphylococcal cutaneous infections who did not respond to these measures were given a course of novobiocin. This was a small group but the results of therapy for the most part were excellent.

Staphylococcic respiratory infections. In this series of Staphylococcus aureus infections, there were 8 patients in whom significant staphylococcal respiratory infections developed (Table I). Three of these 8 patients had fever, cough, and purulent

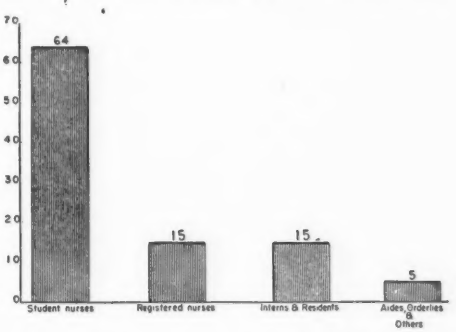

FIG. 3. Personnel with cutaneous staphylococcal infections, February 1956 through January 1957.

sputum yielding Staphylococcus aureus on culture but no evidence of pneumonia. In 4 of the group bronchopneumonia instead of true lobar pneumonia was present. In 1 patient a staphylococcus lung abscess developed. In 4 of the 8 patients the infection developed postoperatively. In 2, endotracheal anesthesia was employed; in 1, spinal anesthesia, and in the other, local anesthesia. Five of these 8 staphylococcic respiratory tract infections were of the problem bacteriophage type 42B/52/81. In all, failure to cough and retained secretions played a role necessitating bronchoscopic aspiration. All the positive cultures were obtained from bronchial secretions. Blood cultures were negative, and in none were metastatic abscesses elsewhere noted. This observation would indicate primary entrance through the respiratory tract. The onset was insidious. There was no chest pain to indicate pleural involvement. Three of the 4 patients with bronchopneumonia died despite employment of antibiotics to which

TABLE III.—NASAL CULTURES OF HOSPITAL PERSONNEL

	Bacteriophage type 42B-52-81		*Other and negative bacteriophage type*		
	No.	*Per cent*	*No.*	*Per cent*	*Total*
Nonpathogenic organisms and coagulase negative staphylococcus albus	—	—	—	—	375
Staphylococcus aureus coagulase positive	11	4	254	96	265
Total					640

the staphylococci were susceptible. It is of interest that this mortality rate is precisely that reported in the presulfonamide, preantibiotic era.

Since resistant staphylococci are found so commonly in the upper respiratory tracts of patients hospitalized for long periods, it is suggested that surgical procedures be accomplished as soon after admission as is practicable. Also recommended are frequent turning, encouragement to cough, and prompt aspiration of retained bronchial secretions in all postoperative patients.

Staphylococcic cutaneous infections in hospital patients not related to surgery. These infections consisted primarily of single or multiple furuncles developing during the patient's hospital stay and were not related to any surgical procedure. There were 58 patients with these infections and 76 per cent of them were infected with an antibiotic resistant staphylococcus of bacteriophage type 42B/52/81 (Table I). It is of specific interest to note that, on several occasions when furunculosis broke out in a ward, it was found that one of the nursing, medical, or ward personnel had a cutaneous infection preceding the ward outbreak in which the identical phage type organism was the responsible agent.

Treatment in these cases consisted of hot, wet dressing and incision and drainage when fluctuation was evident. Hexachlorophene soap was used for bathing and 70 per cent alcohol was used liberally in the involved area. Hospital personnel used 70 per cent alcohol rinses on the hands after bed care of these individuals. Those patients with widespread furunculosis were treated with novobiocin. This therapy was required in only a small group of these patients and the results of treatment in most instances were excellent.

DISCUSSION

Source of the pathogenic organism and its mode of transmission. If a problem of staphylococcal infections is to be dealt with effectively, an epidemiologic study must determine the origin of the organism truly pathogenic for patients and the actual method of spread of that organism. Many authors incriminate various sources and means of transmission of staphylococcus. Perhaps all of the possibilities have been set down by Mitman. It should be realized, however, that nobody has yet proved the true source of the organism or its method of spread. Therefore, these matters still remain in the realm of speculation.

The fact that a healthy member of the hospital staff is found to be a nasal carrier does not mean that that person is the source of an organism which is capable of infecting a patient. Unfortunately, pathogenicity of the staphylococcus is extremely difficult to evaluate in vitro and in vivo even using human volunteers.

Staphylococci have been isolated from dust, air, and bed clothes but this again does not mean that these organisms are pathogenic. At some future date, some investigator might show that, as with the group A streptococcus, the staphylococci in the inanimate environmental reservoir are not pathogenic for men. Elek's experience with inducing staphylococcal infections in human volunteers raises some doubts regarding airborne transmission of staphylococci at the time of surgery. Shooter and associates, who studied airborne staphylococci and reversed the air flow in their operating rooms with positive pressure, recommend that before airborne contamination in surgery is incriminated, all other routes must be excluded.

The nasal carrier in hospital personnel has been incriminated by many as an important source of the pathogenic organism. Our experience with bacteriophage typing of the staphylococci present in these nasal carriers revealed that our problem bacteriophage type (42B/52/81) was present in only 4.1 per cent of 265 nasal carriers (Tables II and III). Yet it was this bacteriophage type which accounted for 50 per cent of the surgical wound infections, 76 per cent of the cutaneous abscesses acquired by patients during hospitalization, and 80 per

cent of the typed organisms from the cutaneous infections in hospital personnel (Table I). It is apparent that nasal carriers of staphylococci in hospital personnel played an insignificant role in the spread of this "problem bacteriophage type" staphylococcus.

We agree with others that one of the most important means of spread of the organism is by direct contact with personnel or patients with active infection or by direct contact with heavily contaminated hospital materials. Hospital personnel may also carry the organisms from infected to uninfected patients if poor technique is used in nursing or medical care of the infected individual. We have had several instances in which certain areas of the hospital were free of infection with staphylococci of bacteriophage type 42B/52/81 until personnel were found on duty with active infection caused by this type of organism. A short time later, these areas experienced their first patient infections. Perhaps airborne dissemination plays some role in the spread of these organisms in the development of clinical infection, but the importance of this role is unknown at the present time. Certainly every effort should be made to control the potentialities of both contact and airborne dissemination in both the hospital wards and the operating rooms.

As Walter and others have emphasized, there has been a relaxation of hospital and operating room techniques during the latter years of the antibiotic era. The medical profession has come to regard the problem of infection much less seriously than it did prior to the development of antibiotics. We are now in an era in which this attitude must be changed. A return to the most strict hospital techniques is essential. Unless this is done, successful control of infections in hospital patients with antibiotic resistant staphylococci is doomed to failure.

Methods of control. The sudden increase in antibiotic resistant coagulase positive staphylococcic infections occurred in our institution early in 1956. A committee on antibiotics was formed at that time and the problem was brought to the attention of the entire hospital staff. The necessity for routine cultures on all patients with infection of any type, whether it be medical or surgical, was re-emphasized to the staff and each of these cases was personally reviewed by the individual committee members. After review, the case was classified. Changes in treatment were recommended when indicated and requested. The bacteriologic survey of hospital personnel and material previously mentioned was undertaken. It was brought to the attention of all hospital personnel that a serious situation had developed, and the necessity for meticulous technique in all departments was strongly emphasized if successful control of these organisms was to be accomplished.

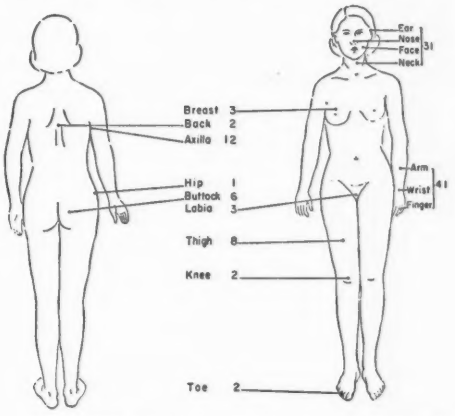

FIG. 4. Site of staphylococcal cutaneous infections in personnel.

Changes in hospital technique. Dressing carriages which were kept in the central supply room and taken out frequently by medical personnel were made available only with a graduate nurse in charge who was well trained in sterile technique. All infected patients were dressed with a special technique in which all dressings and instruments were placed in paper bags and sterilized by steam before cleansing by supply room personnel. We are firmly convinced that dressing carriages should be taken out only with an ex-

perienced nurse in charge if one is to avoid serious breaks in sterile dressing technique.

Attempts at strict isolation of hospital patients with staphylococcal infections were impractical. A modified isolation technique was developed and all bedding and clothing in contact with these individuals were placed in separate, plainly marked bags before transportation to the hospital laundry. The importance of meticulous technique as regards hand washing and alcohol rinses by the hospital personnel after contact with these patients was emphasized. Surgical patients were not placed in semiprivate rooms with any patient with staphylococcal infection. In those wards where there were patients with staphylococcal infection, an attempt was made not to admit patients for elective surgery until control had been established.

Spot checks of the hospital blankets had revealed a number of positive cultures of coagulase positive staphylococci. Due to the rapid turnover of patients, it was found that blankets were not being laundered routinely after individual patient discharge. This was corrected and particular attention was paid to the problem when the discharged patient had had a staphylococcal infection.

Hospital cleaning methods generally were intensified and wet mopping of floors was increased in frequency in an effort to minimize dust.

Hospital personnel with cutaneous staphylococcal infections. These individuals were taken off duty as soon as the infection became evident, and publicity as to the importance of reporting this infection was directed to the attention of all. The majority of these infections were reported by the personnel themselves. In some cases, they were observed by members of the medical staff and the individual was advised as to the importance of reporting the infection. Hospital personnel with cutaneous staphylococcic infections were not allowed to return to duty until all drainage had ceased and there was no evidence of additional infection developing.

Changes in operating room technique. The following changes in operating room technique have been made:

1. The problem was publicized to the operating room staff and the need for meticulous technique was emphasized.

2. Filter type operating room masks were installed, replacing the multiple layer gauze type which had been in use previously. Caps and masks were changed between each operation.

3. The practice of wearing operating room clothing and shoes outside the operating room was forbidden, and all visitors and students were required to change to operating room clothing and shoes before entering the operating room suite itself.

4. Sodium hypochlorite baths were placed in the dressing rooms of the operating room and all individuals entering the suite cleansed the soles of the shoes on these baths prior to entering the suite.

5. Our surgical scrubs were being performed with a liquid hexachlorophene soap. Bacteriologic studies revealed that the stock solution of this soap as received from the manufacturer was sterile. However, the dilutions of this soap dispensed in the operating rooms were found to be contaminated with a coliform organism which had an unusually high resistance to antiseptic agents. The scrubbing technique, therefore, was changed to a 10 minute initial scrub with white soap followed by a thorough rinse with 70 per cent alcohol. Secondary scrubbing between cases if gown and gloves had not been removed was for 5 minutes with white soap followed by thorough 70 per cent alcohol rinse. Occasional hand cultures following this type of preparation were routinely negative for pathogens after 3 hours of operating in rubber gloves. It was our feeling that there had been a steady decrease in the amount of scrubbing time employed by various surgeons and that this was due, in many instances, to the mistaken impression that an antibacterial soap negated the necessity for adequate mechanical cleansing of the skin. It is our strong feeling that the mechanical removal of dirt and

debris from the skin by conscientious scrubbing can never be replaced by 2 to 3 minute scrubs with one of the so-called antiseptic surgical soaps. This is particularly true in operating rooms in teaching institutions where medical students, interns, and student nurses are participating in the surgical procedures.

6. Operating room personnel with any type of cutaneous infection or significant respiratory infection were barred from the operating room. This also applied to patients unless emergency surgery was required.

7. Preparation of the skin of the operative area consisted of (a) cleansing with white soap and scrubbing brush, (b) ether cleansing, and (c) copious application of 70 per cent tinted alcohol solution.

8. In March 1956, it was suggested by the Committee on Antibiotics that a penicillin solution containing 10,000 units of penicillin per cubic centimeter be instilled in all wounds following closure of the fascia with the exception of those in patients who had a history of penicillin allergy and in central nervous system surgery. Clinically, the postoperative wound infections, with a few exceptions, were limited to the subcutaneous fatty tissues. In vitro studies had shown this concentration of penicillin to be lethal to the antibiotic resistant staphylococci. Although it was known that bacitracin and neomycin were more effective agents locally against these organisms, it was difficult to obtain total staff co-operation for the use of these agents because of questions of toxicity. In addition, there was increased expense involved in their use.

This technique was used in approximately 70 per cent of the patients operated upon over a period of 1 year. It is difficult to evaluate accurately the effect of this particular method since multiple changes in hospital and operating technique were simultaneously invoked. One cannot deny, however, that there was a precipitous drop in the instance of wound infection following the institution of this technique in addition to the other changes mentioned (Fig. 2). At the present time, we have stopped instillation of penicillin in all wounds and plan to carry out a control period in an effort to evaluate better the efficacy of this method. We believe that, if the local prophylactic instillation of antibiotics in surgical wounds is required again, we will initiate the use of a solution of neomycin and bacitracin.

9. Patients with established staphylococcic infection requiring surgical drainage in the operating room were scheduled at the end of the operating day. All equipment including linen, was placed in containers and steam sterilized before cleansing. The room was aired and floors and walls were wet cleansed with lysol solution. The room was not used again for 24 hours.

SUMMARY

We have presented our bacteriologic and clinical experience with antibiotic resistant staphylococcal infections in a large general hospital over a period of 1 year. The problem of hospital infections with these organisms is world-wide.

Bacteriophage typing of these organisms revealed that 69 per cent of significant hospital staphylococcal infections were of bacteriophage type 42B/52/81. This figure compares with a 16 per cent incidence of this bacteriophage type organism in patients admitted with staphylococcal infection. Only 4.1 per cent of 265 nasal carriers of coagulase positive staphylococci among hospital personnel were infested with organisms of this bacteriophage type. Thus, nasal carriers of staphylococci among hospital personnel played an insignificant role in the transmission of the organism in our institution. Efforts of control of hospital infections with Staphylococcus aureus must include measures directed with equal vigor toward both airborne and direct contact routes of transmission.

Novobiocin and chloramphenicol are the only two systemically administered antibiotics studied by us to which these organisms are highly susceptible. Staphylococci resist-

ant to both of these antibiotics can and are developing as they have developed after the use of the older antibiotics. The use of novobiocin and chloramphenicol and newly introduced antibiotic agents to which staphylococci are susceptible should be limited to those patients with significant staphylococcal infection whose organisms are not susceptible to any other antibiotic or chemotherapeutic agent and whose infection cannot be controlled by other means such as adequate surgical drainage.

Infections with these antibiotic resistant organisms do not constitute a temporary epidemic but represent a problem which must be faced for an indefinite period of time in our modern antibiotic saturated hospital society. Infected hospital personnel play a dominant role in the transmission of these organisms. The role of the healthy nasal carrier is equivocal. Control of these hospital staphylococci cannot be attained by the discovery of additional antibiotics for resistance to these new agents will probably develop as it has to the ones previously employed. Successful control must be predicated on a return to strict sterile techniques combined with intelligent limitation of the use of antibiotic agents.

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MECKEL'S DIVERTICULUM IN CHILDHOOD

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THE ANOMALY which we now refer to as Meckel's diverticulum was probably first described in 1598 by Hildanus. In 1672 Lavater certainly described it and mention by Rugush, Littre, and Morgagni followed before Meckel adequately described the lesion in 1816 and first recognized its derivation from the omphalomesenteric duct.

EMBRYOLOGY AND PATHOLOGIC ANATOMY

During the third week of intrauterine life, the yolk sac and primitive foregut are continuous. During the fourth week, a separation develops between the gut and yolk sac although the midgut and yolk sac still have only a slightly narrowed margin between them. As both embryo and yolk sac continue to grow, the area of communication remains the same diameter although its length increases greatly to become the slender yolk stalk which remains in the umbilical cord. By the fifth to ninth week, the yolk stalk detaches completely from the midgut and soon degenerates.

The yolk sac blood supply comes through the paired vitelline arteries which later fuse and reduce in number progressively until the only three arterial vessels within the mesentery are the celiac, superior mesenteric, and inferior mesenteric. The terminal branch of the superior mesenteric artery is the omphalomesenteric artery which supplies the omphalomesenteric duct. When the duct persists in any of its forms, the artery frequently remains and is its blood supply.

Arrest of the obliterative process of the omphalomesenteric duct at different stages accounts for the variety of anatomic conditions seen; 24 variants have been described by Evans. When the entire duct remains patent, an umbilical fecal fistula is present. In the most comprehensive review, that of Moses, this occurred in 2.2 per cent of cases reported. Such patency is at times first recognized when ileal mucosa prolapses through the fistula and presents externally.

If the entire duct closes but is persistent, the apex of the diverticulum remains attached to the umbilicus by a fibrous cord. This is said to occur in 10 per cent of all cases and is a frequent cause of a complicating intestinal obstruction.

Only the distal end of the duct may remain open, leaving a blind umbilical sinus lined by intestinal mucosa. If only a small amount of ileal mucous membrane is left at the umbilicus, it may form what is referred to as an umbilical polyp. Very occasionally it can have one or more types of aberrant mucosa within it.

If both ends of the duct close but the central portion remains open, a large, mucus containing cyst may form. This is discovered as an asymptomatic, easily palpable, abdominal mass, but the diagnosis is usually proved only at laparotomy.

By far the commonest variant is the classical ileal diverticulum described by Meckel. This is characteristically located antimesenterically within the terminal 36 inches of ileum. The wall is composed of the seromuscular layers of the small intestine. The mucosa is most frequently ileal in nature, but may have islands of gastric, pancreatic, duodenal, or rarely biliary tract tissue. In some cases, the entire diverticulum is lined by one or more types of this aberrant mucosa. The diverticulum varies from one to several inches in length and the distal end is

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TABLE I.—AGE AND SEX INCIDENCE

	Sex		
Age, yrs.	*Male*	*Female*	*Total*
0–1	33 (14)	9 (3)	42 (17)
1–2	5 (1)	3 (1)	8 (2)
2–3	4 (2)	1	5 (2)
3–4	2	0	2
4–5	0	1 (1)	1 (1)
5–6	6 (3)	0	6 (3)
6–10	9 (5)	5 (2)	14 (7)
10–15	4 (1)	2 (1)	6 (2)
Total	63 (26)	21 (8)	84 (34)

Figures in parentheses are for asymptomatic cases found incidentally at surgery or autopsy.

free in the peritoneal cavity. Occasionally, the free end becomes attached to some other intraperitoneal structure, secondary to inflammation within the diverticulum.

PATHOLOGY

The most common complication of Meckel's diverticulum is hemorrhage. Mild bleeding may occur from inflammation within the diverticulum or secondary to intussusception. If bleeding is moderate to massive in amount, it is almost certainly due to blood vessel erosion by peptic ulceration from heterotopic mucosa. In Moses' review of 1,605 cases, hemorrhage occurred in 30.9 per cent. In most pediatric series, the incidence of hemorrhage is even higher. The bleeding may be episodic and small in amount, or it may be massive and accompanied by profound shock. If heterotopic tissue is present, it is always confined to the diverticulum, a very important point in therapy considerations.

The second most frequent complication is intestinal obstruction (23.8 per cent in Moses' series). This obstruction may be due to intussusception with an inverted diverticulum acting as the leading point of the intussusceptum. A diverticulum attached to another viscus may act as a band which obstructs the bowel, or as a point of fixation around which volvulus may occur.

Perforation of a diverticulum does occur and may be due to inflammation but is more often secondary to peptic ulceration. The clinical manifestations are those of generalized peritonitis, and the correct diagnosis is usually made only at the time of laparotomy.

Uncomplicated diverticulitis is occasionally suspected preoperatively by the localization of pain to the periumbilical region, but, as in perforation, the picture is often not clear-cut, and the "acute" abdomen is opened for "appendicitis."

CLINICAL ANALYSIS

Meckel's diverticulum is the most frequent congenital anomaly of the gastrointestinal tract. Estimates of incidence in the general population vary from 1 to 3 per cent. Skinner and Walters reported a 2 per cent incidence at the Mayo Clinic; Christie reported 63 diverticula in 5,768 consecutive autopsies (1.1 per cent) at New York Babies Hospital. At the authors' hospital, during the period from 1940 to 1955, there was an incidence of 1.32 per cent in 1,809 autopsies.

A condition which occurs this often is worthy of evaluation in terms of the clinical picture and results obtained as well as the methods of treatment which are giving these results. Such an analysis has been carried out here of a series of 84 cases of Meckel's diverticulum from the Children's Hospital of Pittsburgh in which the diagnosis was definitely established during the years from 1940 to 1955. Twenty-one cases were incidental findings at autopsy. Thirteen cases were incidental at the time of operation for other conditions, leaving 50 cases in which the symptoms were attributable to the presence of the diverticulum.

Age and sex. Table I constitutes a summary of the age and sex incidence in this series. Meckel's diverticulum most commonly gives symptoms in patients under 1 year of age; however, the large number under 1 year of age in Table I is weighted somewhat by the number of autopsies in infants with other severe anomalies incompatible with life beyond 1 to 2 weeks of age. Nevertheless, if all incidental cases found at autopsy are omitted, this is still by far the largest group (25 cases). Although the incidence decreases after 1 year of age, it can readily be seen that a significant number of cases continue to occur throughout the

pediatric age range. Males seemed to be more commonly affected in our series.

Presenting complaints of symptomatic cases. The chief presenting complaints in the symptomatic cases included melena in 24 cases, pain in 14, vomiting in 10, and draining sinus in 2 cases.

The melena seen here was most often bright red bleeding, frequently massive in amount. Several patients had a history of previous bleeding episodes, but none had continuing melena for a prolonged period. The finding of melena as the only symptom occurred most commonly in those under 2 years of age.

Pain was most frequently acute and severe, but there were 3 instances of chronic, nagging, periumbilical pain over a period of months. The acute pain occurred most often in the midabdominal area and was commonly diagnosed as acute appendicitis with operation carried out for this reason.

Vomiting, as would be expected, was usually due to intestinal obstruction and was accompanied by other signs of this condition, such as pain, distention, and stool habit change.

The 4 per cent occurrence of umbilical fistula is higher than the usual incidence of this manifestation. It is probably due to chance in this small series.

Operative findings. The operative findings consisted of peptic ulcer in 23 cases, obstruction in 11, diverticulitis in 14, and umbilical sinus in 2 cases. As would be expected in a series with melena as the most frequent complaint, peptic ulcer was the most common operative finding. Frequently, the only gross exterior evidence of ulcer was inflammation of the serosa. Even this was not seen at operation in several cases showing ulcer in the excised specimen. The perforated ulcers had all caused generalized peritonitis at the time of laparotomy.

Intussusception, occurring 6 times, was the most frequent cause of intestinal obstruction, which was usually incomplete. In all 5 cases of obstruction due to volvulus or bands, intestinal obstruction was complete.

TABLE II.—TREATMENT AND RESULTS

	Alive	*Dead*
Diverticulectomy	35 (6)	1
Intestinal resection	21 (3)	1
No treatment	0 (4)	1
Total	56 (13)	3

Figures in parentheses represent incidentally found, asymptomatic cases.

In the group with inflammation the preoperative diagnosis was acute appendicitis with a single exception, a correct preoperative diagnosis of diverticulitis.

Mucosal histology. In 46 of the 50 symptomatic cases, pathologic examination was made of the removed specimens. Twenty-eight (61 per cent) contained gastric mucosa; in 4 of these, other aberrant mucosa was also present. In 17 (37 per cent), only normal small intestine mucosa was present. One specimen showed only granulation tissue.

Of the 34 patients with incidental cases, 1 had gastric mucosa, 9 normal small intestine mucosa, and 24 specimens were not examined microscopically.

Treatment, complications, and results. The results of treatment in this group of cases are presented in Table II. In the 58 operations performed (both symptomatic and incidental groups), diverticulectomy was done 36 times. There was 1 death in this group. The only other complication in this group was 1 case of postoperative enteritis due to Escherichia coli (B4) from which the patient promptly recovered.

Intestinal resection was done in 22 cases, with 1 death in a 6 month old child who had had intestinal obstruction for 48 hours and at operation was found to have intussusception with necrotic bowel which had perforated. One child of this group had an episode of partial intestinal obstruction 1 month postoperatively, from which he recovered without operative intervention. One had marked abdominal distention postoperatively but recovered on conservative therapy. A third child had aspiration pneumonitis and neonatal hepatitis; he recovered and was well, without evidence of any disease, 1 year postoperatively.

The mortality for the entire series in which surgical removal was undertaken (including incidental operative removals) was 3.6 per cent. Treatment was impossible in 1 moribund child who died within 8 hours of admission. If this patient is included, the figure is 4.8 per cent.

There have been no readmissions or clinic visits for recurrent symptoms in this series, including the 4 cases incidentally found in which the diverticulum was not removed.

COMMENT

Symptomatic Meckel's diverticulum occurs relatively frequently in childhood, especially during the first 2 years of life. It is interesting that of the 46 symptomatic cases in which specimens were examined, 61 per cent contained gastric mucosa, while of the incidentally removed specimens examined, only 1 contained gastric cells. In spite of this fact, because of the other complications which are caused by the presence of a Meckel's diverticulum, we believe that all diverticula found at operation should be removed. This belief is given further substantiation by the fact that all deaths in this series were due to severe complications in symptomatic cases. In the incidental cases found and removed at operation, there were no complications which increased the morbidity over that of exploratory laparotomy.

From the fact that occasionally an asymptomatic Meckel's diverticulum is discovered at operation or autopsy in an adult, it is obvious that these diverticula are not all symptomatic. However, the high incidence of symptoms during childhood, the severity of the symptoms, and the deranged physiology make the consideration of this diagnosis imperative in the presence of peritoneal irritation, intestinal obstruction, or melena during childhood. A Meckel's diverticulum should always be thought of if rectal bleeding occurs in patients who are under 2 years of age.

SUMMARY

Eighty-four cases of Meckel's diverticulum are reported and analyzed as to age, sex, presenting complaint, pathology, and type of treatment.

In 36 of 62 cases seen at the operating table, diverticulectomy was performed while in 22 an intestinal resection was done, with an over-all mortality rate of 3.6 per cent. In 4 cases of diverticula incidentally found no treatment was undertaken.

Complications were few and minor; there was no recurrence of symptoms postoperatively.

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A SURVEY OF TONGUE CANCER OVER A FIFTEEN YEAR PERIOD IN A GENERAL HOSPITAL

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THE IMPORTANCE OF CONTINUOUS APPRAISAL of over-all results in the care of cancer patients is self evident. Such appraisal is particularly important in the management of cancer involving the head and neck, in which significant controversy exists as to the relative merits of various methods of treatment. The present communication represents a survey of tongue cancer at the Yale-New Haven Medical Center from 1941 through 1955. A survey of all cases of oral cancer at this institution for the years 1931 through 1940 was carried out by Lawrence and Brezina, a study which has been widely cited as being representative of the experience with this disease in a general hospital, as opposed to the reports from special cancer institutions. It was believed that comparisons between the present study and the Brezina-Lawrence report would be of interest. It is also believed to be important for the general hospital to analyze critically its results for purposes of comparison with those being achieved in the special cancer institutions, as reported by Martin and associates.

BIOGRAPHIC CONTENT

During the period of the study, 91 patients with cancer of the tongue were observed. Seventy-six of these were males and 15 were females. The median age was 65 years, and the age distribution of the patients was as follows: 1 patient was in the group between 31 and 40 years of age, 12 between 41 and 50, 22 between 51 and 60, 32 between 61 and 70, 21 between 71 and 80, and 3 were over 80 years of age. The following number of patients were seen during each year of the study: 5 in 1941, 4 in 1942, 7 in 1943, 5 in 1944, 4 in 1945, 2 in 1946, 8 in 1947, 5 in 1948, 8 in 1949, 6 in 1950, 9 in 1951, 9 in 1952, 8 in 1953, 8 in 1954, and 3 in 1955. Twenty-three of the 91 patients received their primary treatment elsewhere, and of the 68 given primary treatment at this institution, in only 28 patients was there reasonable expectation of cure.

LOCALIZATION OF THE LESIONS

Arbitrarily, the lesions of the tongue were classified in regard to the apparent location of the primary tumor as either anterior or posterior. The latter includes those lesions originating behind the circumvallate papillae. In 35 patients, the lesion was considered anterior and in 56 posterior. After local extension has occurred, oral neoplasms are frequently difficult to ascribe to definite locations. About one-half of the lesions of the anterior part of the tongue had extended to the floor of the mouth, presenting some difficulty in classification. In four-fifths of the posterior cancers, localization was made difficult by extension to fauces, floor of the mouth, anterior part of the tongue, or hypopharynx.

STAGE OF DISEASE WHEN FIRST SEEN

The classification as to the stage of lesions used in this study was that of Harnett and is as follows: stage I, confined to the tongue; stage II, extension to adjacent tissues; stage IIIa, lymph nodes involved—tissues adjacent to tongue not involved; stage IIIb,

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TABLE I.—STAGE OF THE DISEASE WHEN FIRST SEEN

Stage of disease	*No. of cases*	
	Anterior	*Posterior*
I. Confined to tongue	20	7
II. Adjacent tissue involved	2	8
IIIa. Nodes involved, adjacent tissue not	3	7
IIIb. Nodes involved, adjacent tissue also	10	33
IV. Distant metastases	0	1
Totals	35	56

lymph nodes involved—tissues adjacent to tongue involved; stage IV, remote metastases present.

In Table I is shown the number of cases in each of these categories. Noteworthy is the number of patients in whom the disease has progressed beyond confinement to the tongue, particularly in the case of posterior cancers. More than one-half of the patients had cervical lymph node involvement at the time of admission (Table VIII). One patient had distant metastases when first seen. The data concerning the size of lesions when first seen indicate that in 45 patients the diameter was less than 2 centimeters, whereas in 29 it was of a size greater than this, and in 17 the size was not certain.

PATHOLOGY

Among the 35 patients with anterior lesions, all but 3 lesions were definite epidermoid carcinoma. The lesion in 1 patient was diagnosed as "precancerous tumor, grade I," in another patient the lesion was considered to be a rhabdomyosarcoma, and in another instance histologic proof was lacking, and the lesion may have been tuberculosis.

TABLE II.—OVER-ALL RESULTS, 1940 TO 1955

		No. of patients.
Total No. of patients in survey		91
Living without cancer		20
5 years or more	8	
4 years	3	
3 years	1	
Less than 3 years	8	
Dead		71
Without cancer	6	
5 years or more after diagnosis	3	
4 years after diagnosis	2	
2 years after diagnosis	1	
With cancer	65	
Total No. of 5 year survivors		11

Among the 56 patients with posterior lesions, all but 4 lesions were epidermoid carcinoma. Lymphoepithelioma was present in 1 patient, lymphosarcoma in 1, reticulum cell sarcoma in 1, and mixed tumor of the salivary gland in another.

TREATMENT

An organized program was not in effect for the management of oral cancer during the time span covered by this study. The patients included are from both ward and private categories, and for this reason there was considerable variation in their management. Of the 87 patients treated, the majority (72) received irradiation, as: (1) definitive treatment, (2) preoperative treatment, or (3) palliative treatment. About one-third of this number then received supplemental surgical procedures, such as radical neck dissection, excision of the primary lesion after preoperative radiation, and in 6 patients operations were performed for failure of control of the primary tumor by irradiation. In 11 patients irradiation was the treatment given for postoperative recurrence. An analysis of the methods of treatment employed is depicted in Figure 1.

Radiation therapy. Before 1950, external x-ray therapy was used to a great extent in the management of intraoral cancer. The technique was: 200 to 250 kilovolts peak, half value layer 1.5 to 5.0 millimeter copper, skin target distance 50 centimeters, multiple ports through right and left lateral cheeks and submental regions. Occasionally, an additional intraoral cone was used for the lesions located in the anterior part of the tongue and the central floor of the mouth. The daily dose was about 300 to 350 roentgens (air dose) for a total dose of about 6,000 to 7,000 roentgens (tumor dose) in 4 to 5 weeks as a definitive treatment and for a total dose of about 3,000 roentgens (tumor dose) as a palliative treatment.

Radon seeds were used in some instances to supplement the external x-rays, particularly for carcinoma of the posterior part of the tongue.

After 1950, external x-ray irradiation was used as the preoperative treatment in some selected cases for a special study program and is used almost routinely now as preinterstitial radium implantation therapy. It was found that external x-ray treatment alone rarely succeeded in sterilizing carcinoma of the tongue without producing severe damage to the adjacent bone structure; however, it could be used to great advantage as a preliminary step to interstitial radium therapy. An early diminution of the secondary infection and inflammation and a considerable regression in tumor size are usually observed following a preliminary course of external x-ray therapy in the range of 2,000 to 2,500 roentgens (tumor dose). This dose is usually given in a matter of 2 to 3 weeks time using multiple ports, and after a rest period of 1 week, interstitial radium implantation is carried out. In 1942, Richards was among the early investigators to report improvement in his results by administering external roentgen therapy as a preliminary step to interstitial radium therapy.

Interstitial radium therapy has been widely accepted by radiologists to be the most effective form of treatment in the majority of cases of carcinoma of the tongue. If the lesion is small, free from secondary infection, and localized in the anterior part of the tongue, interstitial radium implantation is used in this clinic as the sole form of irradiation treatment for a tissue dose of 7,000 gamma roentgens in 5 to 6 days. If the lesion is larger than 3 centimeters or accompanied by extension to the adjacent tissues, a course of preliminary external x-ray therapy as outlined before is usually given. The interstitial implantation of radium needles is an exacting procedure requiring skill and the proper evaluation of the volume of the potentially neoplastic area. The calculation of adequate dosage requires special x-ray placement films. The Patterson and Parker radium distribution system (6) is closely followed. A biplanar and a pterygoid tongue technique are frequently used.

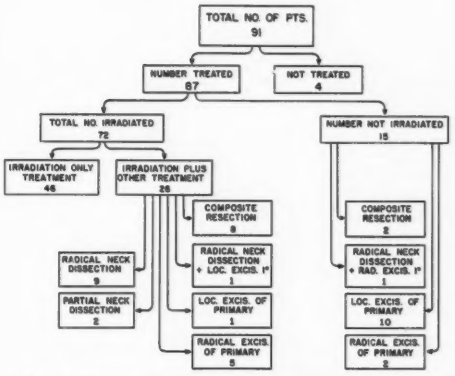

FIG. 1. Diagrammatic representation of the manner in which the series of patients was treated for tongue cancer at the Yale-New Haven Medical Center from 1940 to 1955.

Low intensity radium needles (about 0.66 mgm. per cm. active length) with adequate filtration are essential for producing good results without accompanying complications of soft tissue necrosis. The calculated radium volume dose in our method besides a course of preliminary x-ray therapy is about 4,000 to 4,500 gamma roentgens in 3 to 4 days. The discomfort caused by the procedure is usually quite well tolerated by the patient and is justified by its good results.

In the treatment of metastatic lymph nodes from carcinoma of the tongue, radiotherapy is justified only as a form of palliation after a radical neck dissection has been ruled out. It is our belief that the treatment of choice is radical cervical lymphadenectomy.

Surgical treatment. The number of patients who were subjected to a composite resection is small, 10 patients having undergone such a procedure, in which the involved tongue is

TABLE III.—FIVE YEAR RESULTS IN ALL CASES, 1940 TO 1951

	No. of patients	
Total No. of patients to 1951		54
Living without cancer		8
Dead		46
Without cancer 5 or more years after diagnosis	3	
With cancer or lived less than 5 years	43	
Total No. of 5 year cures		11

Absolute 5 year cure rate, 20.4 per cent

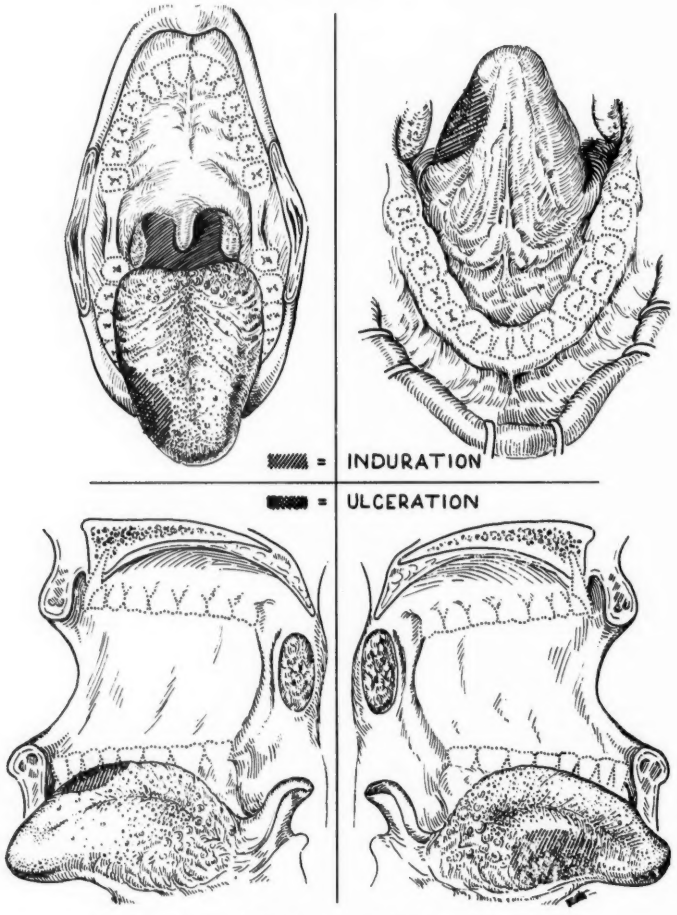

FIG. 2. Diagram indicating the surface of a lingual tumor.

resected in continuity with the ipsilateral cervical lymph nodes, usually with sacrifice of the hemimandible. Such a procedure has also been termed a "commando operation" or a monobloc resection.

In Figure 1, the designation "radical excision of primary" refers to resections of at least the extent of the hemiglossa, whereas "local excision" denotes lesser procedures. The 2 instances of "partial neck dissection" include 1 case in which an upper neck dissection only was done, and 1 in which radical cervical lymphadenectomy was attempted but proved unsuccessful because of the extent of the tumor. One patient who was initially treated by incontinuity resection underwent subsequent neck dissection on the contralateral side. Eleven other patients had radical neck dissections after the primary lesions were controlled by irradiation or surgical excision.

RESULTS

The salvage from this group of patients with tongue cancer is discouraging, as indicated in Table II, which depicts the re-

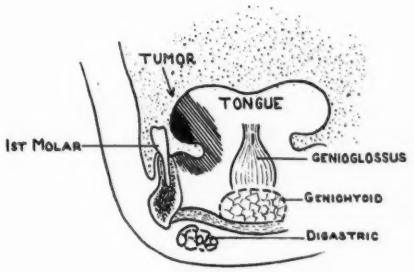

FIG. 3.

FIG. 3. Diagram indicating extent of lingual tumor in coronal section.

FIG. 4. Diagram indicating extent of lingual tumor in saggital or parasaggital section.

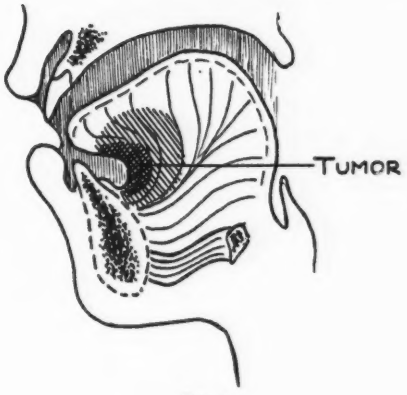

FIG. 4.

sults for the total series, and in Table III, which concerns those patients first seen before 1951. When those patients who received first treatment elsewhere are excluded from the compilation, the survival value for the "primary cases" is seen to be considerably better (Table IV). An attempt has been made in this study to separate those patients in whom the therapeutic efforts were believed to carry an expectation of cure. The number of patients so categorized from the entire series of 91 was 28, which figure is probably inaccurate in the low direction. The significance of the opinion expressed regarding curability is indicated, however, in Table V, which concerns primary treatment for cure, prior to 1951.

Of interest is an analysis of the modalities of treatment employed in those patients who survived 5 years (Tables VI and VII). It is shown that cures result from either surgery or irradiation, alone or in combination. Seven of these 11 patients had stage I lesions confined to the tongue, and in 4 the lesion was less than 2 centimeters in diameter.

Experience with the composite resection for tongue cancer has been limited, consisting of 10 patients, only 2 of whom are living without disease, 1 patient for 4 years and the other for 2 years following diagnosis. Such poor results may reflect the advanced stage of the lesions, since in all but 2 patients cervical lymph node involvement was present at the time of operation, and in most, local extension had occurred as well.

Among the 11 patients who underwent radical neck dissection done not as an incontinuity resection, only 3 are living without disease, 1 for 4 years, 1 for 2 years, and 1 for 1 year after diagnosis. The 1 and 4 year survivors both had metastatic tumors involving the cervical lymph nodes.

TABLE IV.—FIVE YEAR RESULTS IN PRIMARY CASES, 1940 TO 1951

	No. of patients	
No. of patients given primary treatment here		37
Living 5 years or more without cancer	8	
Dead	29	
Without cancer 5 or more years after diagnosis	3	
With cancer or lived less than 5 years	26	
Total No. of 5 year cures		11
Primary 5 year cure rate, 29.6 per cent		

TABLE V.—RESULTS OF PRIMARY TREATMENT FOR CURE, 1940 TO 1951

	No. of patients		
No. of patients given primary treatment with expectation of cure			12
Living 5 years or more without cancer		8	
Dead		4	
Without cancer 5 or more years after diagnosis	3		
With cancer	1		
Total No. of 5 year cures			11
Selected 5 year cure rate, 94 per cent			

DISCUSSION

An attempt has been made to study tongue cancer and its treatment in a general

TABLE VI.—SUMMARY OF TREATMENT IN 5 YEAR SURVIVORS

	No. of patients	
Total No. of patients surviving 5 years		11
Treatment by irradiation only		3
Treatment by irradiation plus surgery		2
Radical neck dissection	1	
Partial neck dissection	1	
Treatment by surgery only		6
Local excision of primary	4	
Radical excision of primary	2	

hospital over a recent 15 year period. It is not an uncommon disease, and among those afflicted the salvage is quite low. To some degree the poor results may represent uncertainty about whether to employ irradiation or surgery in a given patient, and then further uncertainty, once this choice has been made, as to the proper technique for each modality. This fact is particularly true if several different physicians are caring for the patients because none of them sees a sufficient number of cases to acquire adequate knowledge of the natural history of the disease. It is probable that some degree of centralization of care of diseases as problematic as oral cancer results in improved survival figures.

Comparison of the present results with those of Brezina and Lawrence, which covered the years 1931 to 1940, suggests that patients with tongue cancer are not being seen earlier, as evidenced by the fact

TABLE VIII.—CERVICAL LYMPH NODE INVOLVEMENT

	Anterior		*Posterior*		*Totals*	
	No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
No. of patients	35		56		91	
Lymph node involvement*						
On admission	13	37	40	71	53	58
Developed subsequently	5	14	11	19	16	17
Total	18	51	51	91	69	76
Laterality of node involvement						
Ipsilateral only	15		29		44	
Contralateral only	0		0		0	
Bilateral	4		16		20	

*Determined by either histologic findings or strong clinical evidence.

that the incidence of lymph node involvement on admission is the same in both studies. A comparison of these studies with regard to posterior lesions is rendered difficult because of the fact that Brezina and Lawrence grouped the lesions of the posterior part of the tongue and the hypopharynx together.

The 5 year survival figures suggest a slight improvement over the previous time period, but one which porbably does not have statistical significance. It appears then that, in the decades covered, very little improvement has been made in treatment methods. Since the number of patients treated by modern surgical methods is rather small, this study represents a baseline for comparison with the management of future patients managed by more adequate techniques, surgical and radiologic.

TABLE VII.—DETAILED ANALYSIS OF TREATMENT IN THE ELEVEN 5 YEAR SURVIVORS

Case No.	*Patient*		*Tumor*				*Treatment*			*Years survival*
	Age	*Sex*	*Location, ant.*	*post.*	*Size, cm.*	*Stage*	*Definitive surgical treatment*	*Definitive irradiation therapy*		
								X-ray (T.D.)	*Interstitial (T.D.)*	
1	45	M	x		1.5	I		3500 r. 28 days	Radon seeds (3000 gamma r.)	10
2	60	M	x		3.5	II		Ext. & intra-oral 6492 r. 26 days		15
3	72	M	x		2	II		Ext. 5000 r. 21 days	Radon seeds (2000 gamma r.)	6
4	70	M	x		4	I	Part. neck diss. (nodes hist. neg.)	Ext. 6672 r. 13 days	Radium (1760 gamma r.)	7
5	71	M		x	2.5	IIIa	Rad. neck diss. Postirradiation	Ext. 5442 r. 35 days		6
6	63	M	x			I	Local excision			7
7	48	F	x			I	Local excision			16
8	71	M	x			II	Rad. exc. incl. floor and alveolar ridge			5
9	65	M	x			I	Radical excision			5
10	58	M	x		0.5	I	Local excision			10
11	60	M	x		1.25	I	Local excision			6

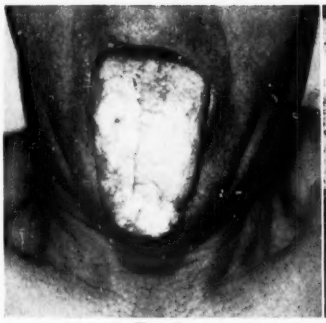

FIG. 5.

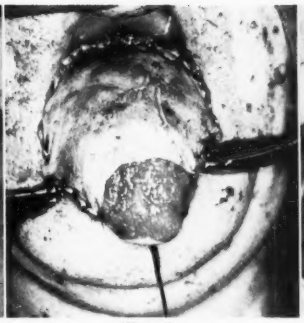

FIG. 6.

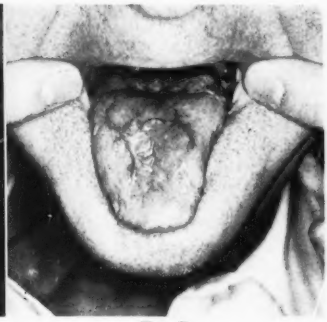

FIG. 7.

FIG. 5. The tongue of a patient with syphilis and extensive leucoplakia.

FIG. 6. Same patient as Figure 5. Photograph taken at operation showing the tongue being resurfaced with a split-thickness skin graft after excision of the leucoplakic mucosa.

FIG. 7. Same patient as Figures 5 and 6. Late postoperative photograph showing skin grafted tongue.

There is little question that small and early lesions can be cured by either good surgery or good radiotherapy. There are, however, questions difficult to answer regarding more advanced lesions. In the moderately advanced tumors, what factors determine the degree to which irradiation or surgery will be utilized? Obviously, the facilities available in each field will influence the decision, but beyond this factor real problems of judgment remain. The surgeon who does not deal extensively with oral cancer, for instance, is rather uncertain as to the exact indications and contraindications for the monobloc resection.

The data available in the literature today as to the superiority of irradiation versus surgery in the treatment of tongue cancer are difficult to interpret, because in reported series there is insufficient effort made to correlate the stage and size of the primary lesion with the percentage of cure. A comparison of two series of patients with a similar stage of disease would be required, one treated by excellent irradiation and the other by good surgical measures. Lacking this information, institutions must use some guess work in arriving at a program for the management of such lesions as tongue cancer. An attempt has been made in the following paragraphs to state the present policy of the University Service of this institution.

Stage I lesions. Small stage I lesions (less than 2 cm. in diameter), particularly if near the tongue border, can be cured by either irradiation or adequate local excision. Preference is expressed for the latter because of the simplicity in procedure and relatively little expense involved. Posterior tongue lesions are seldom in this category of local excisions.

Anterior lesions of moderate size (2 to 4 cm.) may be subjected to adequate local

FIG. 8. A very early tongue cancer, 3 millimeters in diameter, treated by local excision.

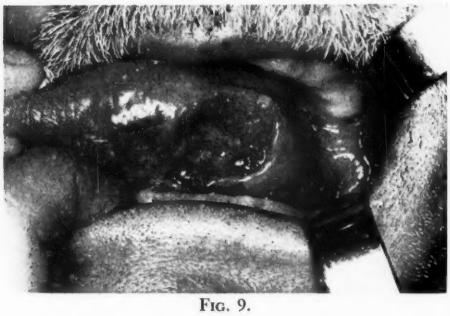

FIG. 9.

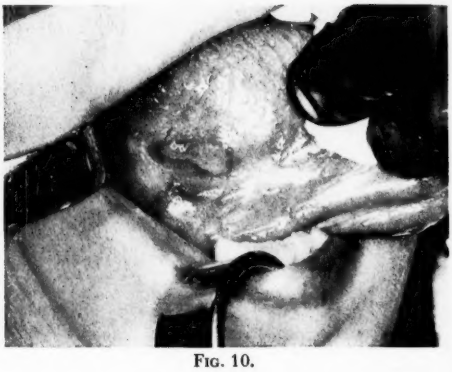

FIG. 10.

FIG. 9. An advanced tongue cancer in a very old man. Treatment was by resection.

FIG. 10. A fairly small cancer of lateral tongue border in middle aged female. Treatment was by irradiation.

excision, with the definition of adequacy being a matter of good surgical judgment, corroborated by the pathologist's findings of a satisfactory margin of normal tissue around the cancer. This adequacy will often constitute hemiglossectomy. In some of the moderate sized lesions, radiotherapy can clear an adequate volume of tongue of the cancer with less loss of substance and less impairment of function than surgery. This choice is a difficult one to make; however, our present trend is toward the more frequent use of irradiation. Lesions near the midline tend to influence the choice in favor of radiotherapy.

Large lesions requiring resection of more than the hemiglossa present enough of a problem regarding closure that resection of the mandible is necessary, with radical neck dissection. The procedure of Kremen, in which the mandible is spared, probably has a place, but this operation has not been employed in the present series. In large lesions frequently there are features present which make surgical curability doubtful, and in these irradiation is the alternative. Occasionally, patients are seen in whom a course of irradiation, given with little hope of cure, is followed by sufficient regression of the primary tumor to permit subsequent successful resection.

Stage II lesions. The extension of tongue cancer to adjacent tissue often means to the floor of the mouth, and, in itself, such extension is interpreted as an indication in favor of the composite operation. Of importance are the results reported by Harrold of the Memorial Center in which a 33 per cent 5 year salvage resulted from this approach utilized in cases of advanced oral cancer. However, if the size of the lesion is small, involving less than 4 centimeters of the tongue and its adjacent tissue, radiation therapy may be used with less deformity and less loss of tissue substance. This is an area which deserves further exploration with radical surgery and with supervoltage irradiation.

Stage III lesions. The presence of cervical lymph node involvement is clearly an indication for radical neck dissection, usually as part of a composite resection, provided that other criteria are met. There have been no instances of bilateral simultaneous neck dissections at this institution.

Very few patients in this series had radical neck dissection as a "prophylactic" procedure, that is, in the absence of clinical node involvement. There probably is a place for prophylactic dissection in certain patients, but this is a matter for individual judgment. Certainly, if metastatic node involvement occurs in a patient whose primary lesion is under control, the indication is for radical cervical lymphadenectomy. Patients with primary lesions treated by

FIG. 11.

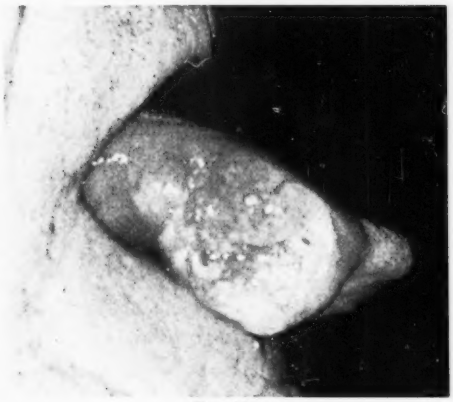

FIG. 12.

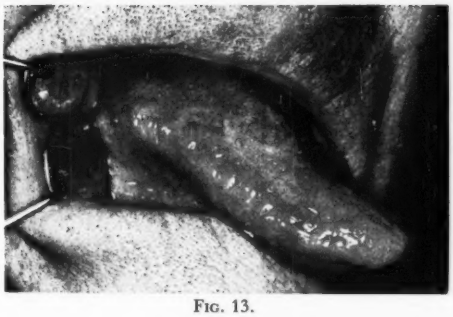

FIG. 13.

FIG. 11. Leucoplakia and cancer of the tongue in a middle aged man with positive serology.

FIG. 12. Lateral view of a large tongue cancer in a patient who was also suffering from uncontrollable laryngeal carcinoma with metastases. The tongue lesion disappeared after irradiation and did not recur.

FIG. 13. A lesion of small size on the dorsum of the tongue in an 80 year old man. Treatment was by irradiation.

irradiation or local excision are carefully followed-up for evidence of failure of control which frequently is an indication for composite resection.

The determination as to which patients are in the category of possible curability may constitute a most difficult aspect of oral cancer management. The attempt to extend resection to patients whose disease is too extensive probably accounts for the low salvage from composite resections in this series and in others. Critical analysis of results from the special cancer institutions, particularly if the lesions are carefully staged, may eventually provide data upon which to base judgments concerning curable operability in a given patient. It is important in making such decisions to have an accurate picture of the extent of the local lesion. There is considerable value in palpation of tongue lesions under general anesthesia, as suggested by Royster, for accurate appraisal of their true extent. The findings are carefully recorded on diagrams, indicating not only surface area covered by the tumor, but attempting to indicate its volume in coronal and sagittal or parasagittal sectional drawings (Figs. 2, 3, and 4).

For various reasons, three-fourths of the patients in our series received irradiation treatment in the management of the primary tongue cancer. In some of these patients the reason was refusal of surgery, and in others it was poor general condition with contraindications for major surgery. In addition, numerous patients have been selected for irradiation therapy because it is our belief that this remains the primary approach to treatment of many tongue cancers. Also, this modality has been of definite value

in a palliative approach to patients with advanced lesions.

Admittedly, considering the limitation of our present knowledge, there exists a degree of uncertainty as to how tongue cancer should be treated, and as to how advances in surgery and radiotherapy should be integrated into our programs of management. It is acknowledged also that factors existing in the relationship between host and tumor may influence the ultimate result as much as the manner of treatment. An attempt has been made, however, to indicate one approach to the questions which exist concerning treatment methods.

SUMMARY

1. A series of 91 patients with cancer of the tongue seen at the Yale-New Haven Medical Center over the period 1940 to 1955 is reviewed.

2. The localization, stage of disease, and size of lesions are discussed. More than one-half of the patients had cervical lymph node involvement on admission.

3. An analysis of the methods of treatment employed is presented. Composite resections were used in a small number of the patients in recent years.

4. The 5 year cure rate for the entire group was 20.4 per cent.

6. The results are discouraging and point out the necessity for improvement in the approach to this problem.

7. A discussion is presented of the factors involved in the choice of methods of treatment and in the relative place of irradiation and surgery.

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CLINICAL EXPERIENCES WITH PHEOCHROMOCYTOMA

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PHEOCHROMOCYTOMA or "black celled tumor" of the adrenal gland has aroused much interest since Labbé and co-workers publicized the association of paroxysmal hypertension and adrenal tumors in 1922. In spite of its notoriety, pheochromocytoma remains a relatively rare tumor, with only about 300 cases having been reported to date. The incidence has been variously determined at 0.4 to 2 per cent of all hypertensives, but some investigators believe the actual incidence to be higher. Graham, using his own and Smithwick's figures, calculated that 600 to 800 people die yearly as a result of untreated pheochromocytoma. These patients represent potentially curable hypertensives, and failure to recognize and treat their disease is lamentable.

In this medical community in the past 4 years, 12 instances of pheochromocytoma have been discovered by either the clinician or the pathologist. This is a striking fact since only 1 patient with this disease is documented in the recorded medical history of this community up to the year 1953. This rather concentrated exposure to pheochromocytoma has allowed us to gain experience in the handling of these patients, and to reach conclusions regarding their management, which, although not new, perhaps need reemphasis. The 9 members of this series about whom we have the most complete data form the basis for this discussion.

CASE REPORTS

CASE 1. W. D., a 29 year old colored female, was first seen in the Emergency Service on March 23, 1956 with complaints of pain in her right side and abdomen and vaginal bleeding. Inquiry into her past medical history revealed occasional headaches which could be relieved by aspirin and lues which had been treated in 1950. There was no indication of past hypertension. Physical examination on that occasion revealed a blood pressure of 140/90, temperature of 99.6 degrees F., pulse 94, and tenderness in the lower abdomen. It was believed that she was suffering from pelvic inflammatory disease. She was seen again on March 27 and 28, 1956 at which time a cul-de-sac aspiration produced blood. She was admitted to the hospital immediately with a diagnosis of ectopic pregnancy.

On physical examination her blood pressure was 118/80, respiration 18, pulse 88. The patient was well developed and well nourished and presented marked right lower quadrant abdominal tenderness and a right adnexal mass. On laboratory examinations the urine was found to be negative; hemoglobin 8.8 grams; packed cell volume 35 per cent; Kahn 3+.

The patient was given .065 gram of soluble phenobarbital and 0.4 milligram of atropine as preanesthetic medication, and at 7:00 p.m. on March 28, 1956 anesthesia was induced with cyclopropane. After induction, the anesthetic agent was changed to endotracheally administered ether and oxygen. The abdomen was explored through a right paramedian incision and a right adnexal mass consistent with the diagnosis of tubal pregnancy was discovered and removed. Blood pressure was maintained in the normal range until 7:35 p.m. when the anesthetist observed a precipitous drop. Anesthesia was discontinued and the patient was given oxygen. Tracheal suction produced pink frothy fluid, and an electrocardiogram demonstrated a pulse rate of 140 with premature ventricular contractions. Intravenous and intramuscular neosynephrine and norepinephrine produced no rise in blood pressure. In addition 125 milligrams of hydrocortisone were given intravenously. Pulmonary edema and respiratory distress increased. Three hours after the initial drop in blood pressure cardiac action ceased. Transthoracic cardiac massage, intracardiac calcium chloride and epinephrine, and electric shock failed to restore cardiac activity. A second electric shock associated with a second injection of calcium chloride restored a regular heart beat. The chest wound was closed. Fifteen minutes after closure no pulse could be detected. The patient was pronounced dead at 12:05 a.m.

The significant findings at autopsy were massive pulmonary edema and atelectasis and a tumor of the

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FIG. 1. Case 1. Photograph of gross specimen showing kidney, tumor, and in upper left hand portion, normal appearing adrenal cortex.

left adrenal gland. The tumor was 7 centimeters in diameter and was seen to displace a major portion of the gland superiorly and medially. It may have risen from extra-adrenal tissue since the point of origin could not be determined with certainty by the pathologist (Fig. 1). The tumor was cellular, soft, and light pinkish-brown in color. Microscopic examination revealed a well encapsulated tumor exhibiting an alveolar pattern of groups of polygonal, granular cells containing vesicular round nuclei. Brown granules typical of the chromaffin reaction were seen in chromate fixed tissue. Examination of the kidneys failed to show evidence of the vascular changes associated with hypertension. The heart was grossly and microscopically normal. The diagnosis was pheochromocytoma.

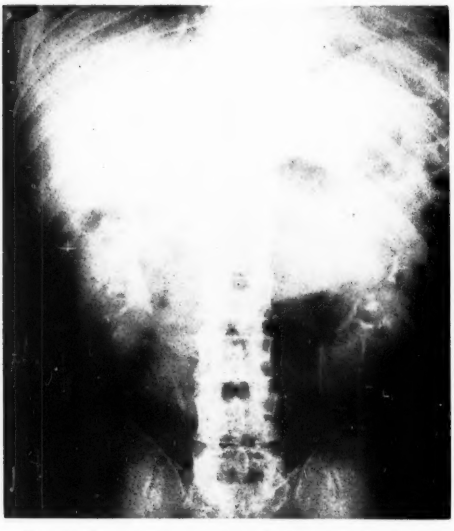

FIG. 2. Case 2. Intravenous pyelogram showing depressed left kidney and attenuated, elongated superior calyx delineating a spherical mass pressing on the kidney.

CASE 2. J. G., a 48 year old white male, had been well until 2 months prior to admission on March 14, 1956. At that time he noted the onset of aching frontal headaches of an intermittent nature not associated with nausea or vomiting. Coincident with the appearance of these symptoms was the gradual loss of visual acuity, especially in the left eye. Paroxysmal hypertension was discovered by his family physician who promptly sought hospital admission for the patient as a pheochromocytoma suspect. The past medical history was significant only in the fact that 2 years prior to admission paroxysmal headaches had been noted by the patient. These had cleared until the observance of the symptoms of the present illness.

On physical examination the blood pressure (sitting) was: right arm 150/100; left arm 140/100; pulse rate 80. There was no postural hypotension. There was definite papilledema bilaterally, worse on the left, with macular stars and hemorrhages. The heart was clinically enlarged with a grade II apical systolic murmur. There were basilar crepitant rales bilaterally, and the liver edge was palpable 3 finger breadths below the right costal margin. On laboratory examinations the urine was repeatedly found to be normal; hemogram normal; phenolsulfonphthalein 40 per cent (20 mins.), 75 per cent (2 hrs.); fasting blood sugar 160 milligrams per cent; eosinophil count 33 per cubic millimeter immediately after operation and 590 per cubic millimeter 1 week after operation. Electrocardiograms showed a wandering pacemaker before operation and normal findings after operation.

The intravenous administration of 5 milligrams of regitine was followed within 3 minutes by a drop in blood pressure from a baseline of 140/100 to 100/70 millimeters of mercury. Conversely, 0.025 milligram of histamine base administered intravenously was followed by a rise in blood pressure from 160/100 to 330+/180 in 1 minute, with the added phenomena of constrictive chest discomfort and severe headache. Five milligrams of regitine were given intravenously when the blood pressure stabilized at 260/150. In 6 minutes the pressure had fallen to 136/98 with the coincident disappearance of all symptoms except a mild headache. An intravenous pyelogram showed a mass distorting the upper pole of the left kidney (Fig. 2). A diagnosis of pheochromocytoma, left adrenal gland, was made.

The patient was explored through a left thoracoabdominal incision. Anesthesia was induced with sodium pentothal and anectine and continued with endotracheal oxygen-ether. A large tumor of the left adrenal gland was removed. Palpatory exploration of the abdomen failed to reveal any other abdominal masses.

It was necessary to give 5 milligrams of regitine intravenously on 1 occasion during operation in order to combat a hypertensive episode. Following removal of the specimen, however, the patient's blood pressure suffered a profound drop and norepinephrine support was necessary for the first 24 hours of the postoperative period. The convalescence was smooth, and a 12 month follow-up examination revealed that the patient was normotensive and had experienced marked improvement in his visual acuity.

On pathologic examination, the specimen measured 10 by 7.5 by 6 centimeters and weighed 297 grams. A splayed-out adrenal gland lay on one surface of the well encapsulated tumor. The tumor substance was pinkish-gray in color and hemorrhagic in areas. Large alveolar nests of polygonal, granular cells characteristic of a pheochromocytoma were seen on microscopic examination. A chromaffin reaction and a positive ferricyanide reduction test were exhibited by the tumor tissue. Figures 3 and 4 demonstrate the gross and microscopic appearance of this tumor.

CASE 3. C. H., a vigorous 26 year old white male, on admission April 24, 1955 gave an 8 to 10 month history of paroxysms of epigastric pain, headache, weakness, nervousness, palpitations, tremulousness, perspiration, and pallor. They were of 5 to 6 minutes' duration and occurred daily or more often. No precipitating cause could be elicited. The patient's physician observed an attack, and noted a labile blood pressure. He subjected the patient to a histamine test and reproduced both the hypertension and the patient's symptom complex. The patient was then admitted to the hospital. On physical examination his blood pressure was 140/90, pulse rate 100. The patient was a well developed, well nourished, white male who exhibited no physical abnormalities. Laboratory examinations indicated urine was negative except for sugar (trace); fasting blood sugar 84 milligrams per cent; basal metabolic rate +11 per cent; hemogram, normal. Intravenous urograms revealed no abnormalities.

There was no postural hypotension. Massage of both flanks and of the abdomen failed to cause a rise in blood pressure. A cold pressor test was negative. A histamine provocative test using 0.025 milligram of histamine base intravenously dramatically reproduced all of the patient's syndrome. It also caused the blood pressure to rise from a pretest level of 140/85 to a maximum level of 250/160 (Fig. 5). A pheochromocytoma was suspected.

The patient was subjected to an exploratory laparotomy under sodium pentothal, nitrous oxide, and ether anesthesia. An initial upper abdominal transverse incision with division of the right rectus muscle was used. The right adrenal area was examined first because of the statistical preponderance of right sided tumors. A "lemon sized" tumor of the right adrenal was discovered. After ascertaining the normalcy of the left adrenal area and the absence of other intra-abdominal tumors, the incision was converted through the ninth intercostal space to a thoracoabdominal incision. The tumor was removed sparing a small portion of the right adrenal cortex. During the opening of the peritoneum the blood pressure rose from 130 systolic to 200 systolic. Five milligrams of regitine was given intravenously with a prompt fall of the blood pressure to normal levels. Regitine in 5 milligram amounts was given on 2 other occasions during operative manipulations to combat blood pressure elevations.

FIG. 3. Case 2. Photograph of gross specimen.

Five milligrams of neosynephrine were administered by intravenous drip in the first 10 hours of the postoperative period as a blood pressure supportive measure. Thereafter the recovery of the patient was uneventful. A follow-up examination 2 years after operation has revealed the patient to be without hypertension and asymptomatic.

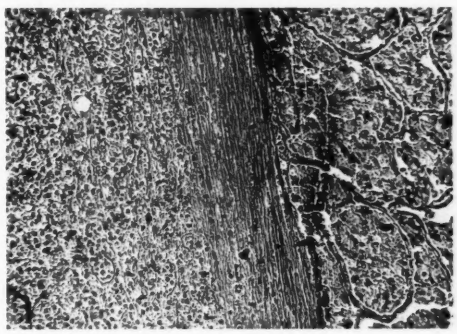

FIG. 4. Case 2. Photomicrograph (×145) of the tumor showing tumor tissue to the right and normal adrenal to the left of the capsule.

On pathologic examination the tumor was found to be an encapsulated mass measuring 4.5 by 4.1 by 2.4 centimeters and grayish-pink in color. The microscopic pattern was one of nests of large polygonal cells with granular cytoplasm and vesicular nuclei. Tumor tissue exhibited the chromaffin reaction with bichromate fixatives. The diagnosis was pheochromocytoma.

CASE 4. M. G., a 36 year old white male truck driver, was well until 1953 when he began to have headaches. A neurologic examination at this time was negative. His symptoms improved only to recur in a more severe form 3 months prior to admission on August 12, 1954. At this time the headaches were occipital in location and associated with nausea and vomiting. The patient's blood pressure which had previously been normal was recorded at 230/150. The initial physical examination in the outpatient department was not remarkable. The blood pressure was recorded as "normal." The headaches were considered "functional" but pheochromocytoma was to be ruled out. A histamine test using 0.1 milligram of histamine base subcutaneously was performed. The blood pressure rose from 170/70 to 220/120. There were associated sweating, nausea, and occipital and coronal headaches. Five milligrams of regitine intravenously promptly lowered the blood pressure. One day later another histamine test, using 0.025 milligram of histamine base intravenously, was conducted with similar results. Roentgenographic examinations of the skull and chest as well as intravenous urograms were negative. The patient was admitted with a diagnosis of pheochromocytoma. On physical examination the blood pressure was 120/78 and 114/78 on 2 determinations. The patient was a well developed young white man with no apparent physical abnormalities. Routine blood and urine examinations were negative; nonprotein nitrogen 30 milligrams per cent; fasting blood sugar 100 milligrams per cent.

A third histamine test using 0.01 milligram of histamine base intravenously was performed with the production of hypertension and symptoms as before. Urine was collected in the posttest period for catechol amine assay. About 14 hours after this test the patient suddenly complained of headaches, nausea, vomiting, and sweating. Blood pressure rose to 250/130. Five milligrams of regitine intravenously controlled the attack. Some hours later the blood pressure was recorded at 190/145 and 10 milligrams of benzodioxane was given with good results. The patient was followed closely, but expired in profound, unmanageable shock the following day.

The urine that had been collected following the last histamine test gave a pressor response when injected intravenously into anesthetized dogs. This was considered to indicate the presence of urinary pressor substances as urine from nonhypertensive patients, serving as controls, failed to cause such an elevation of blood pressure.

On pathologic examination the final diagnoses were acute passive congestion of lungs and liver, and a pheochromocytoma of the left adrenal gland. The tumor measured 3 centimeters in diameter, and was homogeneously grayish-pink in color. Nests of large polygonal, vesicular, granular cells typical of a pheochromocytoma were seen microscopically. A chromaffin reaction was present in tissue prepared in chromate fixative.

CASE 5. F. R., a 51 year old white housewife, first noted paroxysmal occipital and bitemporal headaches, not related to activity, in the fall of 1951. These headaches were usually accompanied by nausea and vomiting. Her physicians informed her of the presence of hypertension at this time. She failed to improve over the course of the next 2 years and was admitted to the hospital May 4, 1953 for evaluation. The past medical history was not remarkable. Her blood pressure was 170/80, pulse 96. The patient exhibited obesity, cardiomegaly, an apical systolic murmur, narrowing of the retinal vessels, and a polypoid lesion of the cervix. Laboratory examinations revealed: negative urine; fasting blood sugar 136 milligrams per cent; hemogram normal.

A cold pressor test caused only an insignificant rise in the systolic and diastolic blood pressures. Histamine (0.05 mgm. intravenously) caused a prompt increase in the blood pressure. Five milligrams of regitine given intravenously at the height of the histamine induced hypertension failed to lower the blood pressure in a prompt manner, although the systolic pressure did revert slowly to pretest levels. A retroperitoneal pneumogram was negative. During this phase of her hospital stay the blood pressure had risen slightly, and she presented a basal blood pressure of 200/100.

The cervical polyp had meanwhile been biopsied and had been found to represent carcinoma in situ of the cervix. It was decided that this condition merited immediate attention even though the presence of a pheochromocytoma was strongly suspected. The patient was subjected to a hysterectomy on May 13, 1953. Anesthetization proved to be a problem with initial attempts to provide satisfactory anesthesia with spinal pontocaine and sodium pentothal drip ending unsuccessfully. Endotracheal nitrous oxide, ether, and oxygen were administered. The uterus and appendix were removed without incident. Because of the suspicion of a pheochromocytoma the abdominal viscera were palpated. There were no abnormalities except in the left adrenal area. Superior, anterior, and medial to the upper pole of the left kidney an irregular mass, roughly 3 centimeters in diameter, was found. The presence of this mass was confirmed by palpation by two members of the operating team. Peritoneal closure had begun when the patient had a generalized convulsion. This occurred 15 minutes after discovery of the suspected pheochromocytoma. Cardiac arrest promptly ensued. Heart massage was instituted following left thoracotomy. Coupled with 2 injections of calcium chloride and 1 of epinephrine, it was effective

in restoring regular cardiac rhythm. The blood pressure at the conclusion of the operative procedure was 120/80, but 4 hours later was 200/100 and 6 hours later was "250/?". Her rectal temperature was noted to be 105 degrees F. a few minutes before she expired.

On pathologic examination the chief anatomic diagnosis was pheochromocytoma of the left adrenal gland. The pathologic changes of hypertensive cardiovascular disease were also noted. The left adrenal tumor measured 9.5 by 6 by 3.5 centimeters and was soft in consistency. Large "brownish" polygonal cells with vesicular nuclei characterized the microscopic picture.

CASE 6.[1] L. A., a 42 year old white male, had been in good health until 4 years prior to admission on January 13, 1954. At that time he contracted a severe headache which lasted for 3 to 4 minutes. The headaches became more frequent and several months later he experienced sudden loss of vision in the right eye. These headaches were posterior in location, throbbing in nature, and not related to any specific inciting incident. A remission of several months' duration occurred, but 3 weeks prior to admission the headaches returned with great intensity. There was now associated nausea and vomiting, and his physician noted increased blood pressure during the attacks.

His blood pressure on admission was 220/130 (130/80 later the same day); pulse 80; temperature 99 degrees F. There was no vision in the right eye, and the left fundus exhibited arteriovenous nicking. The rest of the examination was not remarkable. Flank massage failed to produce hypertension or symptoms. On laboratory examinations, urine showed albumin (trace), sugar (trace); hemogram normal; nonprotein nitrogen 42 milligrams per cent; fasting blood sugar 95 milligrams per cent; glucose tolerance test revealed a diabetic curve. An intravenous urogram demonstrated slight dilatation of the right kidney pelvis with minimal depression of the upper major calyx, but was not considered diagnostic of a suprarenal mass.

A spontaneous hypertensive episode with associated headaches occurred on the first hospital day. The blood pressure was recorded at 230/120 at its high point. Five milligrams of regitine relieved both the hypertension and the symptoms. Histamine base (0.05 mgm.) intravenously caused the blood pressure to rise from 80/40 to 300/150 in 120 seconds. Headache and cold sweating accompanied the pressure rise which was controlled by the intravenous administration of 5 milligrams of regitine. Another similar injection of regitine was required completely to suppress the hypertension. A second spontaneous hypertensive episode occurred on the third hospital day, and this like the first was controlled with regitine. A second histamine-regitine test was also positive. Clinical diagnosis was pheochromocytoma, unlocalized.

Sodium pentothal, nitrous oxide, and oxygen were used to anesthetize the patient for surgical exploration. An upper abdominal transverse incision was first made, and then extended upward in the midline toward the xiphoid. A "grapefruit" sized mass displacing the right kidney was discovered. The tumor was excised leaving a small amount of adrenal cortical tissue behind. Eleven doses of regitine totalling 43.5 milligrams were needed to counteract excessive elevations of blood pressure during the operative procedure. Norepinephrine in small amounts and the Trendelenburg position were used to support the blood pressure for a few hours immediately after operation. In the 3 years since operation the patient has remained asymptomatic and without hypertension.

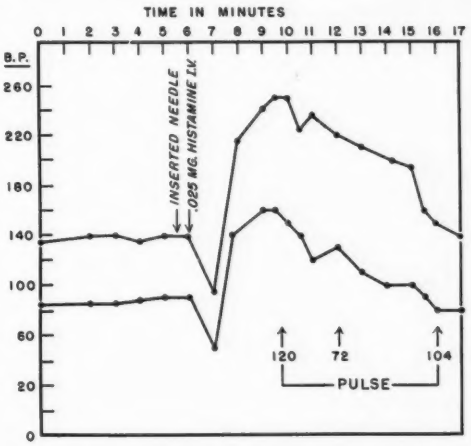

FIG. 5. Case 3. Results of histamine provocative test showing initial fall followed by rise in blood pressure.

On pathologic examination the tumor weighed 282 grams and measured 12 by 8 by 5 centimeters. It was lobulated with a smooth intact capsule. The tissue was yellow to red-brown on cut section, and exhibited areas of necrosis and hemorrhage. The cells presented a pleomorphic picture, but were in general polygonal in shape and contained large vesicular nuclei. Chromate fixed tissue exhibited brownish discolorations of some of the cytoplasmic granules. The diagnosis was pheochromocytoma.

CASE 7. L. D., a 35 year old white housewife, had been well until 1 year prior to her third hospital admission on July 30, 1956. Severe headaches were first noted in July 1955 during the last trimester of a pregnancy which terminated in October with an uncomplicated delivery in another hospital. The headaches continued in the postpartum period. Ten days postpartum, after marked uterine bleeding, the patient went into profound shock and suffered 4 convulsive seizures. She responded well to norepinephrine, cortisone, and transfusion until 2 days prior to her first admission to the St. Thomas Hospital. At this time

[1]This case has previously been reported by one of us (3).

she had another profound hypotensive crisis associated with nausea and vomiting. The condition of the patient during the early days of her hospitalization period was extremely precarious. Her blood pressure was at first unresponsive to norepinephrine administration, but did respond to cortisone. She was discovered to have a Staphylococcus aureous septicemia. Her condition alternated between periods of deep shock and hypertension with blood pressures in the 200/150 range. She gradually improved on oral cortisone and her blood pressure stabilized at normal values. She manifested a persistent tachycardia during her hospital stay, and before discharge complained of hot flashes, nervousness, and intermittent abdominal pain.

The patient was readmitted to St. Thomas Hospital 6 months later complaining of increasingly severe left-sided throbbing headaches. Her personal physician presented evidence for the presence of a labile hypertension. The blood pressure on admission was 130/90, but rose from this level to a value of 260/160 with the intravenous administration of 0.138 milligram of histamine base. Severe headache, restlessness, and hyperhidrosis accompanied the rise in blood pressure. Five milligrams of regitine given intravenously caused a prompt fall in blood pressure and diminution of symptoms. A second histamine test was performed with similar results. One spontaneous hypertensive episode was controlled with 5 milligrams of regitine intravenously. It should be noted that on another occasion regitine, 5 milligrams intravenously, was given at a time when the patient's blood pressure was 125/85, and it was observed that the blood pressure promptly fell to 85/55. Flank massage failed to cause a blood pressure rise and intravenous urograms were normal. The electrocardiogram was normal. A clinical diagnosis of pheochromocytoma was made. Her blood pressure was 120/78; pulse 100. The patient was a well developed, well nourished, white female who showed no apparent physical abnormalities. On laboratory examinations the urine was negative; hemogram normal; basic blood chemical studies normal; basal metabolic rate +24 per cent.

A retroperitoneal pneumogram was performed in a further attempt to localize the suspected tumor, but was interpreted as being normal. Exploration was then carried out. An upper midline abdominal incision was made after the patient had been anesthetized with sodium pentothal, ether, nitrous oxide, and oxygen. A right retroperitoneal tumor was localized by palpation, and removed after the initial incision had been extended into the right ninth intercostal space. Regitine was used twice during the operative procedure to control blood pressure elevations. Norepinephrine was needed to support the blood pressure for the first 50 hours following removal of the tumor. Twelve month follow-up examinations have revealed the patient to be without symptoms or hypertension. On pathologic examination the tumor measured 7 by 5 centimeters and weighed 72 grams. The tissue was soft and grayish-pink in color. There were several areas of hemorrhagic necrosis. The microscopic picture was that of an alveolar arrangement of large, pleomorphic cells. These were bluish-pink in staining reaction, and presented a granular cytoplasm. The diagnosis was pheochromocytoma.

Case 8. C. P., a 53 year old white female, first came under observation at the age of 28 in 1931. She reported to the outpatient department with a 4 years' history of "weak spells," dull throbbing headaches, and high blood pressure. Her blood pressure was recorded at 140/100. Her visits lapsed for 13 years. She reappeared in 1944 complaining of increasing nervousness, smothering spells, tachycardia, blueness of the nails and lips, and excessive perspiration of several years' duration. Blood pressure was 120/85. She had been placed on digitalis 2 weeks prior to this visit by her local physician. This was discontinued as it was thought that her major symptoms were due to digitalis intoxication.

Twelve years passed before she was seen again. She returned to the clinic complaining of 24 hours of vomiting and 2 days of obstipation. She repeated her history of hypertension, claiming systolic levels of 300+, and stating further that her hypertension was not persistent. She also stated that "a small stroke," involving the right side, had been experienced 1½ years before this visit, but had left no residual functional impairment. In addition, 6 years earlier, a cholecystectomy had been performed without incident at another hospital. Physical examination revealed a blood pressure of 90/60, hypertensive retinopathy, and cardiomegaly. The patient had been on antihypertensive medication which had been changed to one of the ganglionic blocking agents 24 hours prior to admission. Evaluation and subsequent clinical course suggested that adynamic ileus on the basis of ganglionic blocking agent intoxication was the cause of her gastrointestinal difficulties. An intravenous urogram made in conjunction with other studies was interpreted as being normal. An intravenous regitine test was performed with a resulting fall in blood pressure from 210/120 to 155/90. The patient was discharged with a blood pressure of 190/100, diagnosed as an essential hypertensive, and placed on conservative antihypertensive measures.

Two months later, October 29, 1956, the patient was readmitted because of the failure of conservative measures to lower her blood pressure. A second positive regitine test had meanwhile been recorded in the outpatient clinic. Blood pressure determinations were in the range of 220/110. She presented grade III hypertensive retinopathy, cardiomegaly, but no abnormal neurologic findings on physical examination. A third positive intravenous regitine test and a negative intramuscular regitine test were obtained. A benzodioxane test caused a blood pressure drop of 60/22 millimeters of mercury. Two subsequent histamine

tests performed on the same day with a basal blood pressure of 190/120 were negative. Urine was collected for catechol amine assay, and the patient was discharged on raudixin, phenobarbital, and a low salt diet. The catechol amine assay was found to be 800 micrograms per day (upper limit of normal 200 μgm. per day). The patient entered the hospital for the third time on an emergency basis because of the onset of generalized convulsions on December 9, 1956. Her blood pressure was 180/115; pulse 80. The patient was semistuporous and exhibited continuous tonic convulsions of the right side of the body. Marked hypertensive retinopathy was noted. Cardiomegaly was present and there was an apical systolic murmur. Weakness of the right one-half of the body was evident. The urine showed 1+ protein and was otherwise negative; hemogram normal; fasting blood sugar 83 milligrams per cent; nonprotein nitrogen 28 milligrams per cent.

The patient's sensorium cleared spontaneously once the convulsions had been controlled by sedation. Re-evaluation of the intravenous pyelogram taken 2 months previously indicated the distinct possibility of a mass overlying the right kidney. Exploration without undue delay was deemed advisable and was performed December 14, 1956. Sodium pentothal induction with ether maintenance constituted the anesthetic management. A right thoracoabdominal incision provided access to a 7 by 5 centimeter right adrenal mass which was readily removed. Palpation of the abdominal contents failed to reveal any other abnormal masses. Contrary to expectations, the blood pressure manifested a consistent tendency to fall throughout the operative procedure. Norepinephrine was needed to maintain an acceptable blood pressure level during operation and for 72 hours of the immediate postoperative period. Convalescence was complicated by the appearance of a superficial skin slough over the cutdown site in the leg through which the norepinephrine had been administered. The patient was discharged with a blood pressure of 130/90. Subsequent follow-up evaluations over a 6 month period have shown a gradual rise of blood pressure until values approaching preoperative levels have been obtained. Repeat intravenous urograms, and a repeat regitine test, have been normal.[2]

Pathologic examination showed the tumor to be a well encapsulated mass measuring 7 by 5 by 5 centimeters and weighing 137 grams. Microscopic examination showed a rim of normal adrenal cortical tissue surrounding a large mass of pleomorphic polygonal cells with granular cytoplasm and eccentric vesicular nuclei. The tissue fixed in Orth's fluid gave an excellent chromaffin reaction. The pathologic diagnosis was pheochromocytoma.

CASE 9. J. F., a 60 year old white male, had experienced headaches and dizziness for about 6 months before admission on February 21, 1957. His family physician had discovered an elevation of blood pressure. The patient had noted no cardiopulmonary symptoms, but had suffered from occasional "indigestion" and pain in the left side. The past history was noncontributory. His blood pressure was 170/100. The general physical examination showed no significant abnormalities. There were no palpable abdominal masses, and no postural tachycardia or hypotension. Upon laboratory examinations the urine was negative; hemogram normal; nonprotein nitrogen 46 milligrams per cent; fasting blood sugar 95 milligrams per cent.

Five milligrams of regitine given intravenously caused the blood pressure to drop from its basal value of 170/100 to 130/74 in 2 minutes. An electrocardiogram showed nonspecific T wave changes. An intravenous urogram revealed marked depression of the left kidney with the presence of a right-angle bend in the ureter and poor filling of the calyceal system (Fig. 6). The clinical diagnosis was pheochromocytoma of left adrenal gland.

Preoperative preparation included 50 milligrams of regitine by mouth on the morning of operation. Anesthesia consisted of sodium pentothal induction with nitrous oxide and oxygen supplemented by anectine. A left thoracoabdominal incision was used, and a large cystic left adrenal tumor was found. The tumor was adherent to the spleen and left kidney and these organs, as a consequence, were sacrificed. Because of the adhesions the tumor was inadvertently ruptured during removal. Therefore it was not possible to measure the volume of the contained fluid. Large amounts were evacuated by suction and it was noted that the tumor originally filled the major portion of the left upper quadrant.

Operative manipulations resulting in blood pressure elevations necessitated the use of 40 milligrams of regitine during the procedure, and norepinephrine was required to support the blood pressure once removal of the tumor had been accomplished. The fluctuation of the blood pressure and its response to both regitine and norepinephrine are well illustrated by the anesthesia record (Fig. 7).

Although norepinephrine and levophed were needed for the maintenance of an adequate blood pressure for the first 4 postoperative days, the patient's blood pressure required no support for the first few hours in the recovery room. This may have been an expression of a pressor effect resulting from the absorption of the unevacuated tumor fluid. The blood pressure was 120/80 when the patient was discharged from the hospital and has remained normal in the 4 months since operation.

Pathologic examination showed that the gross specimen consisted of the left kidney, spleen, and the collapsed walls of the cystic tumor. Adrenal cortical tissue could not be recognized with certainty. Accurate microscopic identification of a pheochromocy-

[2]Postoperative urinary catechol amine values have not been elevated.

FIG. 6. Case 9. Intravenous pyelogram showing depression of left kidney and angulation of left ureter.

toma was hampered by the presence of scarring and necrosis, but tissue with the typical alveolar arrangement of large granular cells was found in one area and diagnosed as a pheochromocytoma.

DISCUSSION

The clinical syndrome of the functioning pheochromocytoma with paroxysmal hypertension, headaches, sweating, pallor, lability of the vasomotor mechanisms, vertigo, nausea, and vomiting has been widely described since 1922. As experience has accumulated various other hypertensive symptom complexes associated with this tumor have been recognized. It is now appreciated that the pheochromocytoma may give rise to clinical manifestations which simulate any of the hypertensive disorders. It is also apparent that a pheochromocytoma may exist in a clinically dormant state or may be associated with signs and symptoms of such subtlety as to go unrecognized until a catastrophe occurs (Case 1).

In general two groups of hypertensive symptoms are found. Goodall and Symington have classified them as follows:

Group I. A. Paroxysmal hypertension with normal blood pressure between paroxysms.
B. Paroxysmal hypertension with raised blood pressure between paroxysms.
Group II. Persistent hypertension without paroxysms.

The associated phenomena are paroxysmal or persistent as the case may be. Present evidence indicates that the paroxysmal manifestations are seen in relatively early stages of the disease while persistent symptoms may signal a process of long duration. This has been explained on the basis that continued direct action of the vasospastic substances produced by the tumor converts a paroxysmal disorder into a chronic one propagated by other than these humoral mechanisms. This concept offers an explanation for the refractory hypertension exhibited in Case 8 after a fairly well documented illness of 29 years' duration.

In addition to the element of time, the nature of the vasospastic agent produced by the tumor seems to influence the symptom complex. Goldenberg and associates correlated clinical manifestations and tumor catechol amine content and reached the following conclusions:

1. The total epinephrine and norepinephrine content of the tumors is essentially the same in both persistent and intermittent hypertension.
2. Tachycardia, hypermetabolism, and hyperhidrosis are a part of the clinical picture of patients with persistent hypertension, if the tumor produces predominantly epinephrine.
3. Small tumors which produce chiefly norepinephrine give rise to symptoms similar to those of essential hypertension.

In general it was thought that a sympathomimetic response was characteristic of epinephrine activity, and that an essential hypertensive response was characteristic of norepinephrine activity.

The paroxysms have been analyzed by Graham and Smithwick among others. The attacks seem to occur with increasing frequency as the disease progresses (Case 6).

The duration between attacks can vary from minutes to months, and the duration of the individual attack may be measured in seconds to days. Graham observed that severe attacks frequently followed periods of inactivity. He postulated that the patient, while active, was subjected to many subclinical vasopressor discharges but that resumption of activity after a period of rest allowed the tumor to discharge a large, "stored-up" amount of the vasospastic agent into the circulation with resultant clinically recognizable symptoms. A variety of triggering stimuli for the production of attacks have been described and include laughing, leaning to the side of the tumor, tight girdle, physical exercise, urination, and sexual intercourse.

The problem of the "asymptomatic" pheochromocytoma is difficult to evaluate. Blacklock's group reported an incidence of 11.8 per cent in their review of 141 cases. The tumor may function at a subclinical level or may be manifested only by hyperglycemia, being activated under conditions of stress as already indicated. In addition the tumor may exist in a dormant state between paroxysms for varying periods of time and its true level of activity not be appreciated.

The term "pheochromocytoma" is usually reserved for tumors of chromaffin tissue occurring at or near the adrenal gland. Tumors with histologic characteristics similar to those of pheochromocytoma have been described in the brain, carotid body, and sympathetic chain, but are generally classified as "paragangliomas." Tumors in extra-adrenal locations are more likely to be hormonally inactive, and it has been proposed that these be called "chemodectomas." Grossly, pheochromocytomas are usually well encapsulated, fleshy tumors of yellow-brown or reddish-brown color. Often an attenuated adrenal gland can be seen overlying a portion or all of the tumor. On cut sections the tissue is usually grayish-pink and characterized by hemorrhage, necrosis, and cyst formation. A thin 1 to 3 millimeter zone of typical yellow adrenal cortex may be seen. Microscopically the structure is somewhat variable. The cells are usually large, polyhedral, or irregularly shaped with granular, slightly acidophilic cytoplasm, and a large eccentric vesicular nucleus. For the most part the cells are arranged in an alveolar pattern, but this is not constant. One group has classified the tumors into small alveolar, large alveolar, and intermediate types. Pleomorphism, lymphatic, blood vessel, and capsular invasion frequently occur and cannot be considered signs of malignancy. Distant metastases alone provide the justification for such a conclusion.

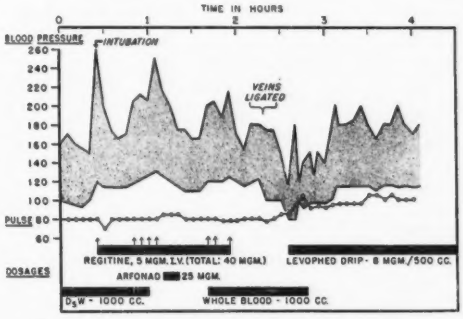

FIG. 7. Case 9. Anesthesia record showing lability of blood pressure during operation and response to regitine and norepinephrine.

The tumors vary widely in size and weight—the largest on record weighed 2,000 grams with its contained cystic fluid. The usual weight range is from 1 to 75 grams with variation from 1 to 15 centimeters in diameter. The size of the tumor cannot be positively correlated with severity of symptoms.

Right sided lesions are more common than left sided tumors in a proportion variously estimated at 2 to 1, and 3 to 2. The reason for this is unknown. Multiple tumors have occurred in about 11 per cent of the reported cases and about 74 per cent of multiple tumors are bilateral—an over-all incidence of bilaterality of 7 to 8 per cent. Bilateral tumors exhibit a higher incidence

of malignancy than single lesions. The bilaterality of pheochromocytomas may therefore have some prognostic significance.

Any patient with a medical history suggestive of hypertension and hypermetabolism, without hyperthyroidism, but with good renal function should be subjected to critical evaluation for a pheochromocytoma. The treacherous nature of this disease, as indicated by our own clinical experience as well as that of others, demands that this evaluation be carried out in the hospital under strict supervision and without undue delay. It is only in this way that patient salvage can be increased. As previously stated, the disease may well be more prevalent than present case reports would indicate.

The search for confirmatory evidence of the presence of pheochromocytoma should begin with the physical examination and serial recordings of the patient's blood pressure. An abdominal mass may rarely be palpable. More often palpation over the site of the tumor will cause hypertension, tachycardia, and symptoms even if the tumor itself is not felt, but even here the evidence may be misleading as pheochromocytomas have been found on the side opposite from that indicated by the palpatory findings. Postural tachycardia, postural hypotension, and peculiar vasomotor phenomena such as blueness of lips, nose, and finger nails, pallor, flushing, coolness of extremities, and lowering of skin temperature are not unusual in this disease and their presence or absence should be elicited.

Assessment of renal status is the next logical step in evaluation for two reasons: (1) It may demonstrate the basis of the hypertension; (2) It provides information that enables the surgeon to exercise intelligent judgment in dealing with the kidney during surgical exploration. A by-product of the investigation of renal function may well be the localization of the tumor on the intravenous or retrograde pyelograms.

Laboratory examinations are usually directed at defining the degree of hypermetabolism. The most frequently noted chemical abnormality of the blood is an elevated fasting blood sugar. This may be intermittent or persistent and may be associated with glycosuria and a diabetic type of glucose tolerance curve. This can lead to an erroneous diagnosis of diabetes mellitus although the two conditions may coexist. The basal metabolic rate is often elevated in patients with pheochromocytoma. This is less likely to be so in the presence of essential hypertension where Graham and Smithwick found basal metabolic rates above +20 per cent unusual. In this series 2 patients (Cases 2 and 5) demonstrated an elevated fasting blood sugar; one (Case 7) exhibited a basal metabolic rate of +24 per cent; and one patient (Case 6) showed a diabetic type of glucose tolerance curve with glycosuria. Thus 4 of the 9 patients manifested some evidence of hypermetabolism.

The conclusive proof of the presence of a pheochromocytoma rests with the demonstration of elevated levels of circulating epinephrine or norepinephrine in the blood or of their excretion products in the urine. Until quite recently this was in large measure impractical. Only indirect pharmacologic testing based on either potentiating or diminishing the effect of the suspected circulating vasopressor substances was available. The indirect approach to the diagnosis of pheochromocytoma was initiated by Roth and Kvale (13) in 1945 when they devised the histamine provocative test. This test has its greatest application in those patients who exhibit paroxysmal hypertension with normotensive intervals. A cold pressor test is first carried out in order to assess blood pressure lability (this is usually normal in patients with a pheochromocytoma); then 0.05 milligram of histamine base in 0.5 cubic centimeter of normal saline is given intravenously. A positive reaction is indicated when the pressure rise is 60/40 above the patient's basal values. The test is not without danger and should not be performed on patients with a blood pressure of 170/100 or higher. Goldenberg and associates (9) reported an accuracy of 97 per

cent with positive histamine tests and 88 per cent with negative histamine tests. The reliability of this and other pharmacologic tests has also been assessed by Evans and associates.

The alternative indirect approach is to block the effect of circulating vasopressor substances. This is both safer and more comfortable for the patient. Several drugs have been used but regitine, an adrenergic blocking agent, is considered the drug of choice. The regitine test is useful mainly in the presence of hypertension and a positive test constitutes a blood pressure drop of 35/25 within 2 minutes after an intravenous dose of 5 milligrams of the drug. The injection of regitine into pheochromocytoma suspects who exhibit normal basal blood pressures, as in Case 7, is not recommended as occasionally a precipitous and irreversible fall in blood pressure may occur. However, this fact does indicate that pheochromocytoma patients may become dependent on the secretions of their tumor for maintenance of normal vascular tone. The accuracy of the regitine test is almost 100 per cent in excluding pheochromocytoma when negative reactions to the intravenous test occur. A positive reaction to a properly conducted intravenous regitine test has been 90 per cent accurate in Goldenberg's hands (9) and 96 per cent accurate in the experience of Roth and Kvale (14). Because of the margin of error, when positive regitine tests are recorded, the results should be confirmed by additional testing with benzodioxane. Positive regitine tests should be considered invalid if sedatives, narcotics, or antihypertensive drugs have been administered within 48 hours of the test. Uremia has also been indicted as the basis for false positive reactions.

Our testing experience based on these 9 cases shows no false negative regitine tests in 13 determinations, but 3 false negative histamine tests in 15 such examinations. Only 2 benzodioxane tests were run and these were considered positive.

In recent years the estimation of urinary catechol amine content has become widespread, and in effect has superseded pharmacologic testing in definitive diagnosis. Goldenberg and associates (9) in this country and von Euler and co-workers in Sweden (4, 5, 6) have developed practical methods for urinary catechol amine assay. A high catechol amine excretion rate was observed consistently by these investigators in patients with pheochromocytoma, and was noted in the 1 patient of the present series on whom preoperative assays were performed (excluding Case 4 in which only qualitative biologic assays were carried out).

Catechol amine assay has not, however, proved infallible, but at the present time these tests provide the safest and most reliable means of confirming the clinical suspicion of a pheochromocytoma. The danger of repetitive testing and of treating these patients as pharmacologic curiosities is well illustrated by the patients in Cases 4 and 8. Where possible, in the future, it is our intention to minimize indirect pharmacologic testing and to rely more heavily on the determination of urinary catechol amine excretion.

Once the presence of pheochromocytoma has been established, the supplementary problem of localization of the tumor arises. Palpatory evidence may provide the answer if a mass is found or if pressure in a particular area of the abdomen is followed by tachycardia and an elevation of blood pressure. Localization by physical examination was not possible in any of our patients and this seems to mirror the most frequent experience of others. The intravenous urogram, as in Cases 2, 8, and 9 may demonstrate the tumor but more than likely will not as Kvale and Roth's 20 per cent success indicates (12). Laminography at times is helpful. Aortography and retroperitoneal pneumography are additional measures that can be resorted to in the effort to visualize the tumor. As a general rule, these procedures introduce hazards which are probably not justified by their results and which may be avoided by a well planned surgical

approach. There is, as yet, no diagnostic substitute for adequate exploration.

Preoperatively, minimal stress to the patient is desirable. Regitine may be valuable in those pheochromocytoma suspects with persistent hypertension. It is essential that both epinephrine blocking agents and pressure supporting drugs be available during operation. Regitine and norepinephrine, respectively, are the most valuable agents. It is our preference to prevent dangerous elevations of blood pressure by the use of repeated small doses (5 mgm.) of regitine as necessary during induction of anesthesia and conduct of operation rather than to use a continuous intravenous infusion of the drug.

We believe with Apgar and Papper that the anesthetic regimen of choice is sodium pentothal induction with ether, nitrous oxide, and oxygen maintenance. Cyclopropane has the property of sensitizing the myocardium to epinephrine and should be avoided. The hypotensive effects of spinal anesthesia are sometimes difficult to control while sodium pentothal or nitrous oxide alone do not give the necessary muscular relaxation. Curare has been noted to have a histamine-like effect on these patients and its use is not recommended. As a general principle, anoxia, which stimulates the adrenal gland, is to be assiduously avoided. It is also best if anesthesia can be induced in the operative position as undue movement of the patient is thus avoided.

The choice of incision is governed by the position of the tumor, when this is known or strongly suspected. In such instances we favor a thoracoabdominal incision utilizing the eighth or ninth intercostal space on the side of the tumor with the patient placed in a semilateral decubitus position on the operating table. In those instances in which preoperative localization of the tumor is inexact, we believe that an initial upper midline or transverse abdominal incision which can then be extended to give the proper thoracoabdominal exposure is preferable. The necessity for gentle handling of the tumor, early ligation of the veins, and careful search for multiple or peculiarly located tumors has previously been stressed. No attempt to spare adrenal cortex at the site of the tumor should be made as the danger of increased manipulation of the tumor and the possibility of implantation of tumor cells overbalance the disadvantage of total unilateral adrenalectomy. In most instances after removal of a pheochromocytoma, norepinephrine or another vasopressor agent is required to combat a hypotensive state. An intravenous infusion of dilute norepinephrine may be necessary for 24 to 72 hours after operation. Postoperative blood pressure support was required by all 6 of the patients explored for pheochromocytoma. The duration of this support varied from 10 hours to 4 days.

The fact that there have been no deaths in this series in those patients in whom the preoperative diagnosis or suspicion of pheochromocytoma was followed by a specific surgical procedure designed to discover and remove the tumor attests to the validity of the concept of approaching this disease with dispatch and singlemindedness of purpose.

CONCLUSIONS

An evaluation of the 9 cases presented, together with a consideration of the nature of the disease, leads to certain conclusions.

1. Pheochromocytoma is probably more prevalent than is generally believed. A higher index of suspicion coupled with a more efficient use of diagnostic aids is necessary if the salvage rate of this group of potentially curable hypertensive patients is to be raised.

2. Classically, the manifestations are paroxysmal in nature, but this may be expected in only slightly more than 50 per cent of the patients. Hypermetabolism is usually, but not necessarily, clinically apparent.

3. Indirect pharmacologic tests aimed at altering the effects of the circulating vasopressor substances produced by the tumor have been the principal methods of confirming clinical diagnosis since 1945.

4. Direct estimation of urinary catechol amines should supplement and may eventually supersede the indirect tests in confirming clinical diagnosis since the direct method is safe and is a potentially more accurate approach to the problem.

5. Pheochromocytoma is a treacherous tumor and delay in surgical treatment may be fatal. In untreated patients, death usually results from cerebral hemorrhage, myocardial infarction, or pulmonary edema. Once the diagnosis is made it is important to move with alacrity to definitive treatment. In view of the treacherous nature of the disease it would appear unjustifiable to delay surgical treatment for any considerable period merely to multiply pharmacologic tests.

6. There have been no deaths in the present series when definitive surgery for preoperatively recognized pheochromocytoma has been carried out, and we believe that the reported operative mortality rate of 15 to 20 per cent for this disease will be lowered in the future.

7. The reports of others indicate a 50 per cent mortality rate in patients who harbor a pheochromocytoma and are subjected to unrelated major surgical procedures. The surgical treatment of pheochromocytoma should, therefore, take precedence over the treatment of other coexisting conditions except in severe emergencies. Our own experience confirms this viewpoint, as well as demonstrating the inadvisability of performing surgical diagnostic maneuvers when not fully prepared to combat complications engendered by these maneuvers.

8. The anesthesia of choice must permit rapid induction, adequate oxygenation, and relaxation with minimal vasomotor alterations. These aims can be accomplished by the use of sodium pentothal induction with nitrous oxide, ether, and oxygen maintenance.

9. The surgical approach which provides best exposure of the tumor is in our opinion a thoracoabdominal one. When the location of the tumor is not known with certainty an initial abdominal incision should be planned so as to permit its conversion into a thoracoabdominal exposure after the tumor has been localized and the search for multiple foci of tumor formation completed. Gentle handling of the tumor during its removal and the immediate availability and intelligent use of blood pressure regulating drugs are essential.

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THE EFFICACY OF ANTIBIOTICS COMBINED WITH IRRIGATION IN EXPERIMENTAL STRANGULATED INTESTINAL OBSTRUCTION

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ALTHOUGH MUCH PROGRESS has been made in recent years in the treatment of intestinal obstruction, the results obtained in those cases complicated by strangulation leave much to be desired, as shown by Nemir and associates. In spite of the administration of fluids, electrolytes, blood, suction, and resection of necrotic bowel, an irreversible downhill course is too often the result.

The importance of bacterial factors in experimental strangulated intestinal obstruction has been recently emphasized by Cohn. There was a significant prolongation of life in those animals that received antibiotics directly into the strangulated loop.

The peritoneal cavity has been shown to be the site of accumulation of large amounts of dark, foul fluid late in the course of this disease. This material was found to be lethal for normal dogs in amounts as small as 3 cubic centimeters per kilogram (1). These experiments also showed that aspiration of the fluid from the peritoneal cavity after a standard time interval yielded no better results than those obtained in untreated animals. Thorough irrigation of the peritoneal cavity in another group receiving the same dose and after a similar time interval significantly improved the survival time. The purpose of the following experiments was to determine the effects of antibiotics alone and in combination with peritoneal irrigation upon normal dogs which had received peritoneal fluid from animals dying of strangulated intestinal obstruction.

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MATERIALS AND METHODS

All animals. Sixty unselected adult mongrel dogs were used for these experiments. Anesthesia was induced by the intravenous injection of nembutal. Sterile technique was utilized for all operative procedures.

Donor animals. Peritoneal fluid was obtained from 7 animals dying of strangulated obstruction of a 15 centimeter segment of ileum. Following ligation of the mesenteric veins and marginal vessels, a tie of umbilical tape was placed around each extremity of the segment to be strangulated (Fig. 1). The abdominal wounds were closed and the animals were placed in their cages. At or shortly before death, the peritoneal fluid was removed and kept in a refrigerator until it was used.

Recipient animals. Peritoneal fluid from the donors was injected directly into the peritoneal cavity of normal animals. One liter of saline, which had been warmed to body temperature, was used in all animals which received irrigation of the peritoneal cavity. The 53 recipient animals were divided into two groups.

Group 1.—These animals (11) did not receive penicillin. They were given 3 cubic centimeters of fluid per kilogram of body weight, and in 3 animals it was not removed. Peritoneal lavage was effected in 4 animals after 10 minutes and in the remainder after an interval of 20 minutes.

Group 2.—In this group of animals (42) a dose of 600,000 units of penicillin was injected into the muscle of the thigh at the time the fluid was delivered into the peritoneal cavity. A similar dose of penicillin

was also given 24 hours later. Four animals of this group were given 3 cubic centimeters of fluid per kilogram of body weight. Irrigation of the peritoneal cavity was carried out in 2 after a 10 minute interval, while the fluid was not removed from the others. Thirty-eight animals were given intraperitoneal fluid in the amount of 5 cubic centimeters per kilogram of body weight, and it was not removed from 8. The remaining animals received peritoneal lavage after 10 minutes (2 dogs), 20 minutes (4 dogs), 30 minutes (8 dogs), 45 minutes (8 dogs), and 60 minutes (8 dogs). Animals living 3 days were considered survivors.

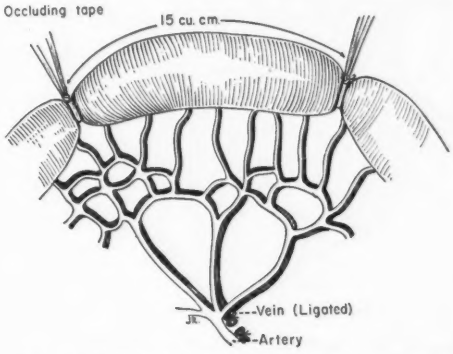

FIG. 1. Method of producing intestinal strangulation.

RESULTS

Donor animals. The average length of life after operation in these animals was about 34 hours. They moved about their cages actively until 2 to 3 hours before death. Their downhill course was at this time characterized by a rapid respiratory rate, lethargy, and coma. Three to five hundred cubic centimeters of dark, foul fluid were removed from the peritoneal cavity of each animal.

Recipient animals. Group 1.—Although irrigation prolonged life, there were no survivors among those animals (11 of them) which did not receive penicillin (Tables I and II).

Group 2 (received penicillin).—All animals (4) which received 3 cubic centimeters per kilogram survived even though the fluid was not removed from the peritoneal cavity. The remainder of the animals received 5 cubic centimeters per kilogram, and in those from which the fluid was not removed (8) there were no survivors. All animals survived that received irrigation of the peritoneal cavity after 10 minutes. The same was true for those irrigated after 20 minutes. Seven of 8 animals survived when irrigation was effected after 30 minutes, while 5 of 8 animals recovered when the interval was 45 minutes. Only 3 of 8 animals survived when irrigation was postponed for a period of 1 hour.

DISCUSSION

The precise lethal fraction of peritoneal fluid resulting from strangulated intestinal obstruction has not been defined. The bacterial content of this material was considerable, and it is reasonable to assume that bacterial toxins were also present. The products of hemoglobin breakdown do not appear to be lethal agents in themselves.

There are, of course, many factors involved in the determination of whether or not an animal will survive an episode of strangulated intestinal obstruction. The detrimental effects of fluid, electrolyte, and blood loss, as well as complications incident to resection and anastomosis of gut, were

TABLE I.—RESULTS IN ANIMALS GIVEN PERITONEAL FLUID WITHOUT ATTEMPTS AT REMOVAL

No. of animals	*Amount given, c.c./kgm.*	*Penicillin*	*Survivors*
3	3	0	0
2	3	+	2
8	5	+	0

TABLE II.—RESULTS IN ANIMALS WHICH RECEIVED PERITONEAL IRRIGATION AFTER INJECTION OF FLUID

No. of animals	*Amount given, c.c./kgm.*	*Time fluid remained in peritoneal cavity, mins.*	*Penicillin*	*Survivors*
2	3	10	+	2
4	3	10	0	0
4	3	20	0	0
2	5	10	+	2
4	5	20	+	4
8	5	30	+	7
8	5	45	+	5
8	5	60	+	3

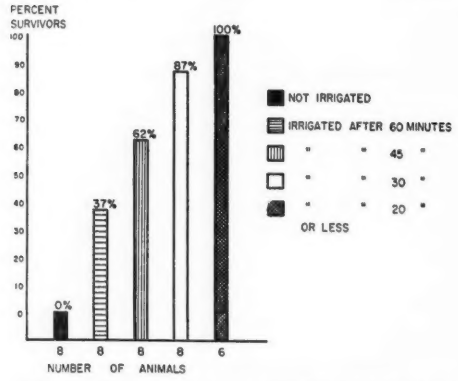

FIG. 2. Comparison of survivors in animals which received 5 cubic centimeters of fluid per kilogram, showing effect of peritoneal irrigation on penicillin treated dogs.

eliminated by injecting the fluid directly into the peritoneal cavity of the normal animals.

It was apparent early in the course of this work that penicillin alone would protect animals against doses as large as 3 cubic centimeters per kilogram. When 5 cubic centimeters per kilogram were given it was necessary to irrigate the peritoneal cavity, and the sooner this was done the better were the animals' chances for survival (Fig. 2). It is probable that the lethal fraction of this fluid gradually builds up in the blood stream until irreversible changes occur in vital centers. This question is the concern of investigative work in progress at the present time.

CONCLUSIONS

1. Penicillin protected normal dogs against an otherwise lethal dose of 3 cubic centimeters of strangulation fluid per kilogram.
2. Penicillin did not protect normal dogs against the lethal effects of 5 cubic centimeters of fluid per kilogram.
3. In combination with penicillin, irrigation of the peritoneal cavity increased the percentage of survivors when the larger dose was given.
4. The sooner irrigation was effected after injection of fluid, the better were the animals' chances for survival.

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THE USE OF SERUM FREEZING POINT DEPRESSIONS IN EVALUATING SALT AND WATER BALANCE IN PREOPERATIVE AND POSTOPERATIVE STATES

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IT IS OFTEN DIFFICULT to evaluate the state of hydration and electrolyte balance in the surgical patient. Measures which have been used include the patient's weight, urine output, and the serum sodium level. If an excess of water is given there will be an increase in weight, and similarly if a progressive water deficit occurs the patient's weight will fall. Careful weighing of the patient with an accurate bed scale will eliminate many serious problems of water balance. On the other hand, accurate weights, particularly in bedridden patients are difficult, if not impossible, to obtain and they give no indication of the level of the serum electrolytes or accumulation of organic or inorganic wastes from poorly functioning kidneys.

An adequate urine output usually means adequate fluid and electrolyte balance. However, overhydration may be overlooked, particularly in the presence of renal disease, if one depends solely on the urine volume. Even more perplexing is the problem of decreased urine output in the postoperative period. Is more fluid required or is renal insufficiency developing?

Serum sodium is quite constant in the normally hydrated patient and usually is recorded as 140 ± 3 milliequivalents per liter. With such a highly reproducible serum sodium level in normal hydration, the level of serum sodium is a good indication of excess water loss or overhydration, the sodium rising and falling in these conditions respectively.

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In addition, the freezing point depression[1] of serum provides useful information in the elucidation of fluid and electrolyte problems. The serum freezing point can be determined in a few minutes using only 2 cubic centimeters of serum, and this same 2 cubic centimeters of serum may then be used to determine the serum sodium level by flame photometry. The manner in which serum sodium values when correlated with the freezing point depression of that serum may be helpful in evaluating fluid problems is demonstrated in the examples which follow.

MATERIALS AND METHODS

All sodium determinations were done by using a Barclay flame photometer with lithium as an internal standard. The freezing point depressions of the serum were done with a Fiske osmometer on 2 cubic centimeters of serum and are expressed in degrees centigrade and milliosmols. Studies with the Fiske osmometer have indicated a a highly stable freezing point depression of the serum. The freezing point depression of the serum in the postabsorptive state of 25 patients without evidence of fluid or electrolyte imbalance studied by us was −0.54 degrees C. (290 milliosmols) with a standard deviation of −0.014 degrees C. (9 milliosmols). This is in agreement with Smith and with our previous determinations of the freezing point depressions using a Beckmann thermometer (3). Of the many physical properties of solutions the freezing point depression

[1]Freezing point depression is obtained by determining the freezing point of the serum and expressing the value in degrees centigrade below zero. This value can also be expressed in milliosmols using the factor 1,000 milliosmols=1.86 degrees C.

TABLE I.—RELATIONSHIPS OF SERUM SODIUM AND SERUM FREEZING POINT DEPRESSION (Δ^t)

	Serum Na	Δ^t *serum*	*Suggested treatment*
Dilution hyponatremia (excess intake of water)	Low	<—0.51° C. (274 mosm.)	Restriction of fluids
Sodium depletion (true loss of total body Na)	Low	Normal range between —0.51° C. (274 mosm.) and —0.55° C. (296 mosm.)	3 per cent NaCl intravenously with concomitant restriction of water
Underlying renal disease	Normal or low	>—0.56° C. (301 mosm.)	Treatment of underlying disease
Primary water loss	High	>—0.56° C. (301 mosm.)	Give large amounts of glucose in water preferably i.v.
Chronic cellular hypo-osmolarity	Low	<—0.51°C. (274 mosm.)	No treatment indicated

Mosm., milliosmols.

TABLE II.—EXAMPLES OF DILUTION HYPONATREMIA

Patient	*Clinical course*	*Fluids*	*Sodium*	Δ^t*°C.*	*Comment*
T.W.	88 yr. old W/F Transverse colostomy for obstructive diverticulitis of the sigmoid	In the first 5 postoperative days patient rec'd 8,000 c.c. of glucose in water and 4,000 c.c. of glucose in saline intravenously	123 mEq./L. on the 5th postoperative day	—0.50 (269 mosm.)	On the 5th postoperative day fluids were restricted and during the next 7 days patient rec'd only 2,000 c.c. of glucose in saline. Na slowly rose to 135 mEq./L. and freezing point returned to —0.53°C. (285 mosm.)
W.J.	58 yr. old W/M Exploration and closure of perforated peptic ulcer	Rec'd 19,000 c.c. of glucose in water and 2,000 c.c. amigen intravenously in the first 8 postoperative days	122 mEq./L. on the 8th postoperative day	—0.47 (258 mosm.)	Fluids restricted and although two further surgical procedures were done Na rose to 138 mEq./L. and freezing point depression of serum returned to —0.53° C. (285 mosm.) 13 days after the restriction of fluids
A.O.	92 yr. old W/M Transverse fracture of the right humerus treated with Jones collar and cuff and developed bronchopneumonia while in the hospital	Rec'd 5,000 c.c. of glucose in water and 2,000 c.c. of glucose in saline intravenously first 4 days in the hospital	126 mEq./L. on 5th hospital day	—0.48 (258 mosm.)	Fluids discontinued intravenously and patient was allowed to take water by mouth ad lib. 12 days later Na had risen to 138 mEq./L. and freezing point returned to —0.55° C. (295 mosm.)
A.F.	82 yr. old W/F Exploratory laparotomy with lysis of adhesions	First 5 postoperative days patient rec'd 9,500 c.c. glucose in water and 6,500 c.c. glucose in saline intravenously	126 mEq./L. on 5th postoperative day	—0.48 (258 mosm.)	Intravenous fluids stopped on 5th postoperative day and 5 days later Na rose to 133 mEq./L. freezing point fell to —0.51° C. (274 mosm.)
K M.	78 yr. old W/M Choledochostomy with removal of stones	Rec'd 4,500 c.c. of glucose in water and 1,000 c.c. of glucose in saline first 3 postoperative days	117 mEq./L. on 3rd postoperative day	—0.46 (248 mosm.)	Fluids restricted and Na rose to 130 mEq./L. 9 days later with a freezing point of —0.51 °C. (274 mosm.)
E.E.	61 yr. old W/F Cholecystectomy and common duct exploration	Rec'd 5,000 c.c. of glucose in water and 2,000 c.c. amigen and 1,000 c.c. saline in first 3 postoperative days	122 mEq./L. on 3rd postoperative day	—0.49 (264 mosm.)	Fluids restricted and given only by mouth ad lib. Na rose to 132 mEq./L. in 2 days and freezing point decreased to —0.52° C. (278 mosm.)

(usually recorded as Δ^t) is one of the most constant. The freezing point is lowered 1.86 degrees centigrade for every gram molecular equivalent of glucose in 1,000 grams of water and the freezing point depression is a measure of the number of particles in the solution.

EXAMPLES

CASE 1. M. C., a 72 year old white female, was admitted to the hospital for removal of bilateral cataracts. The physical examination was not remarkable with the exception of a mild hypertension of 160/90. Three days after admission and under local anesthesia, an intracapsular cataract was removed from the right eye. Two days following surgery the patient

developed diarrhea consisting of 4 or 5 loose, watery stools per day and was placed on chlorpromazine, 25 milligrams intramuscularly twice a day, phenobarbital, 30 milligrams twice a day, and codeine, 30 milligrams twice a day. At that time it was thought that the patient was not drinking enough water, and she was given 2,000 cubic centimeters of levugen and 500 cubic centimeters of normal saline daily for the next 5 days (Fig. 1).

During this time the patient became progressively lethargic, unresponsive, and the blood pressure fell to 110/70. Finally she lapsed into a coma. At that time electrolyte studies revealed a serum sodium of 116 milliequivalents per liter, chloride of 85 milliequivalents per liter, nonprotein nitrogen 36 milligrams per cent and bicarbonate 24 milliequivalents per liter. The freezing point of the serum at this time was −0.47 degrees C. (253 milliosmols) indicating a marked dilution. The patient was thought to have a dilution hyponatremia, and to be showing the clinical picture of severe water intoxication. Fluids were abruptly reduced and the patient slowly regained consciousness, became responsive, recovered after 7 days, and was discharged from the hospital. Serum sodium level slowly rose to 138 milliequivalents per liter, chloride to 106 milliequivalents per liter, and bicarbonate to 23 milliequivalents per liter, and the final serum freezing point was −0.52 degrees C. (280 milliosmols).

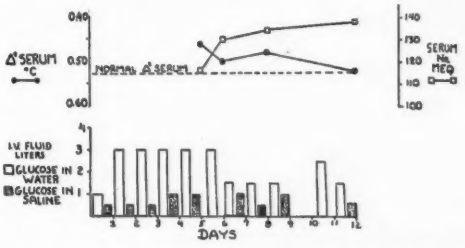

FIG. 1. Case 1. Dilution hyponatremia. Note elevated freezing point of serum −0.47 degrees C. (253 mosm.) and low sodium 116 milliequivalents per liter on the fifth postoperative day after large amounts of electrolyte-free fluids administered intravenously indicating increase in water over solute in extracellular fluid compartment. Restriction of fluids from sixth to twelfth postoperative day resulted in a rise of sodium to 138 milliequivalents per liter and fall in freezing point to −0.52 degrees C. (280 mosm.) with recovery.

Table I indicates four possible states of sodium and water imbalance. It will be noted that, in overhydration or so-called "dilution hyponatremia," the serum sodium is low (usually below 130 mEq./L. of serum) and the freezing point of the serum is above −0.51 degrees C. (274 milliosmols) usually between −0.44 degrees C. (236 milliosmols) and −0.50 degrees C. (269 milliosmols) indicating a lower solute concentration in the serum. This is the most common type of water and electrolyte imbalance seen in the postsurgical patient in this hospital. It is often called "dilution hyponatremia," "water intoxication," "primary water excess," or "dilution acidosis." These are all names for the same entity—that is, an increase in total body water with consequent dilution of all the electrolytes and nonelectrolytes dissolved in the body water. Additional examples of dilution hyponatremia are given in Table II.

The best treatment for this situation is prevention. Many investigators have pointed out that in the postsurgical state patients cannot handle a water load. Water in any form, but particularly intravenously, should be given with caution for the first 24 to 36 hours following surgery especially in the older patient. Once dilution hyponatremia has developed, water should be limited or withheld until water loss from the kidneys and insensible sources restores the sodium and the freezing point to normal. This may take several days as shown in Case 1. The use of isotonic saline is not indicated in this condition as there is no primary sodium deficit—only an excess of water—and the addition of isotonic saline only aggravates the condition. These patients are similar to camels who can go for several days without water as they are carrying a large, excess reserve. In severe cases 5 per cent sodium chloride may be given intravenously with restriction of water in an attempt to restore normal tonicity to the extracellular fluid compartment and promote diuresis.

CASE 2. F. C., a 73 year old white male, was admitted to the hospital from home with a history of having fallen. Physical examination showed an acutely ill, poorly nourished, thin, white male. Blood pressure on admission was 100/70, pulse was 88 per minute, and temperature was 102.4 degrees. The patient was confused. Pupils were small but reacted to light. Chest showed bilateral basilar rales and the conditon of the heart was not remarkable. The abdomen was soft and nontender with no masses, and bowel sounds were present. There were no lateralizing neurologic find-

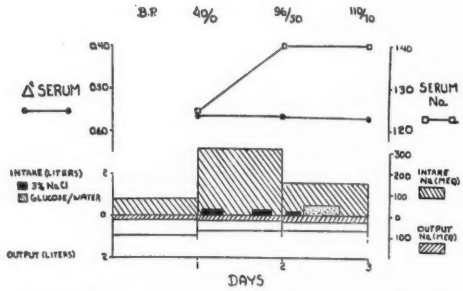

FIG. 2. Case 2. Salt depletion. The serum sodium is 124 milliequivalents per liter and freezing point depression of the serum −0.56 degrees C. (301 mosm.). Improvement followed intravenous administration of hypertonic sodium chloride with concomitant limitation of water. Note rise in serum sodium to 140 milliequivalents per liter without change in freezing point depression.

ings. X-ray examination revealed a fracture of the right fourth, fifth, sixth, seventh, and eighth ribs in the posterior axillary line and of the ninth, tenth, and eleventh ribs in the right scapular area. There was a transverse fracture of the neck of the right humerus with medial displacement of the distal fragment.

Hemoglobin was 10 grams, white blood count 23,000 per cubic millimeter with a left shift. Urinalysis showed specific gravity of 1.015, albumin 0, and an occasional red and white blood cell per high power field.

It was thought that the patient had an associated bilateral bronchopneumonia. He was placed on penicillin, 200,000 units intramuscularly twice a day. During the first 3 hospital days the patient had a daily temperature of 102 degrees orally. The weather was very hot and the patient perspired profusely requiring several changes of bed linen daily. Because the patient appeared "dehydrated" a total of 5,000 cubic centimeters of levugen and 3,000 cubic centimeters of 5 per cent glucose in saline was given intravenously during the first 4 hospital days (Fig. 2).

During this time the patient became semicomatose, unresponsive, and on the fourth hospital day the blood pressure, which had been steadily falling, was recorded as 40/0.

Electrolyte studies on this day showed nonprotein nitrogen of 83 milligrams per cent, chloride 92 milliequivalents per liter, bicarbonate of 15.6 milliequivalents per liter, sodium 124 milliequivalents per liter, potassium 4.5 milliequivalents per liter, and the freezing point depression of the serum was −0.56 degrees C. (301 milliosmols).

On the basis of the clinical picture, the large amounts of electrolyte-free fluid administered, and the profuse perspiration, the patient was considered to have a primary salt-depletion. All fluids were stopped and the patient was given 600 cubic centimeters of ' per cent sodium chloride intravenously over the next 18 hours (Fig. 2). Improvement was noted after a few hours. The patient's sensorium became clear and his blood pressure in 24 hours was 96/50. After 48 hours the blood pressure was 110/70, nonprotein nitrogen was 56 milligrams per cent, chloride 113 milliequivalents per liter, bicarbonate 20 milliequivalents per liter, sodium 140 milliequivalents per liter, potassium 3.9 milliequivalents per liter, and the freezing point depression of the serum was still −0.56 degrees C. (301 milliosmols).

True salt depletion occurring in preoperative and postoperative patients has been very rare in our experience. It occurs more frequently in medical practice in such cases as salt-losing nephritis, Addison's disease, and excess sweating with free access to water. However, occasionally a patient who has intestinal intubation may have a low serum sodium and chloride due to removal of salt in excess of water. Case 2 demonstrates a depletion in body sodium and chloride secondary to profuse sweating with concomitant administration of electrolyte-free fluids. It will be noted in this case and in Table I that even with low serum sodium values the freezing point of the serum stays within normal range in true salt depletion. Exactly what is maintaining the serum osmolarity in salt depletion is not known. However, animal experiments suggest that the formation of osmotically active substances probably by the kidney sustains the serum osmolarity within the normal range during salt depletion. In these cases the administration of hypertonic sodium chloride with concomitant limitation of water intake will quickly restore the serum sodium value to normal and will bring about improvement in the patient's condition. The response of salt depleted patients to intravenous or oral hypertonic sodium chloride is one of the most gratifying in medical practice. Improvement occurs often within a few hours with clearing of the sensorium, rise in blood pressure, decrease in pulse rate, and general improvement. Unfortunately, many of the patients do not improve because the physican or surgeon does not limit

water during the time he is administering hypertonic sodium chloride. This is somewhat surprising in view of the fact that the essential physiology of this condition was worked out many years ago by Darrow and his co-workers (1, 2). With true salt depletion there is a shift of extracellular water into the cell with consequent cellular overhydration. The administration of hypertonic sodium chloride draws this water out of the cells and establishes normal cellular hydration. The simultaneous administration of water with the hypertonic sodium chloride defeats the purpose.

CASE 3. A. M., a 66 year old white male, was admitted to the hospital critically ill with a history of vomiting for the previous 3 weeks. On the evening of admission, the patient vomited bright red blood 6 times. Past history was not remarkable except for the fact that the patient was told he had "liver disease" 25 years before.

Physical examination revealed an acutely and chronically ill white male. Blood pressure was 120/80, pulse 120 per minute and thready, the respirations were 24 per minute and regular. The skin was warm and dry. Examination of the head and neck revealed no unusual findings. The lungs were clear to percussion and to auscultation. The heart was not enlarged, tones were distant, there were no murmurs. The liver was felt 4 fingerbreadths below the costal margin and was tender. No other masses were felt in the abdomen and black feces were found in the rectum.

It was thought that the patient was bleeding from esophageal varices and a Sengstaken tube was inserted. In spite of 15 blood transfusions, the patient continued to show signs and symptoms of continued blood loss. On the third hospital day the upper abdomen was explored under pentothal-ether-oxygen anesthesia. Exploration revealed a large liver and a gallbladder filled with stones. Exploration of the stomach revealed a small ulcer approximately 1 centimeter in diameter which was quite thick, and believed to be a carcinoma. A small, bleeding vessel was seen in the ulcer. Subtotal gastrectomy with a Billroth II anastomosis was performed and 2 needle biopsies of the liver were obtained. The patient remained somewhat confused after surgery and the blood pressure rose to 242/104. Signs of congestive heart failure became apparent on the second postoperative day. This was treated with digitalis and oxygen. On the fourth hospital day it was found that the patient had a serum sodium of 128 milliequivalents per liter, chloride 95 milliequivalents per liter, and a nonprotein nitrogen of 120 milligrams per cent. Freezing point depression of the serum was −0.57 degrees C. (306 milliosmols).

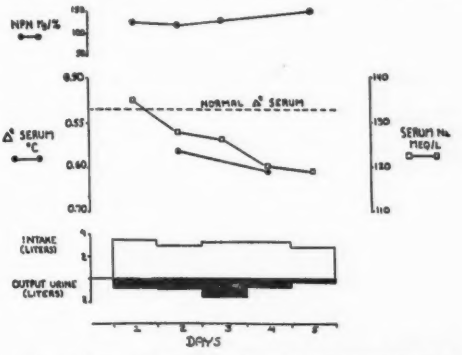

FIG. 3. Case 3. Hyponatremia with hyperosmolarity of the extracellular fluid compartment. Sodium 128 milliequivalents per liter on second postoperative day with lowering of freezing point of serum to −0.57 degrees C. (306 mosm.). In spite of 3 to 4 liters per day of intravenous glucose and water, fourth postoperative day shows sodium 119 milliequivalents per liter and freezing point depression of serum to −0.62 degrees C. (333 mosm.). Autopsy showed replacement of kidney tissue by anaplastic carcinoma of the lung.

It was believed that this represented an impairment of kidney function with an increase in tonicity of the body water and a decrease in serum sodium. The patient continued to deteriorate, and although large amounts of 5 per cent glucose in water and 5 per cent glucose in saline were administered, sodium continued to fall to 119 milliequivalents per liter, on the day of death. At that time the nonprotein nitrogen was 141 milligrams per cent and the freezing point depression of the serum was −0.62 degrees C. (333 milliosmols) (Fig. 3).

Postmortem examination revealed a highly anaplastic carcinoma of the lung with metastasis to the stomach, liver, and both kidneys. Both kidneys were almost completely replaced with tumor tissue.

Occasionally following surgery a patient will have a rising nonprotein nitrogen, decreased urinary output, and a low or normal serum sodium due to a decreased kidney function causing a high concentration of solute in serum water with a marked lowering of the freezing point of the serum.

Case 3 is a case in point and shows the significance of an increase in serum tonicity manifested by a progressive lowering of the freezing point and a fall in the serum sodium following surgery. Such circumstances should directly suggest intrinsic renal disease. The cause of the low serum sodium frequently

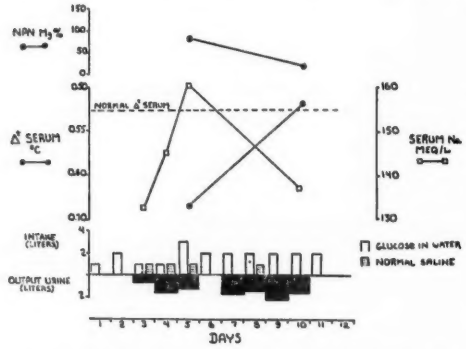

FIG. 4. Case 4. Primary water loss. Sodium of 158 milliequivalents per liter on fifth hospital day with lowering of the freezing point of the serum to −0.67 degrees C. (360 mosm.) indicating loss of water and increase of solute. Following 5 per cent glucose in water intravenously and oral fluids the sodium fell to 136 milliequivalents per liter and freezing point of serum returned to normal −0.54 degrees C. (290 mosm.).

accompanying marked derangement of kidney function is obscure. It has been suggested that it is due to an intracellular sodium shift or to dilution of the extracellular fluid volume. Of all types of electrolyte imbalance in preoperative and postoperative patients, this is the most serious and the finding of a markedly lowered freezing point of the serum and a low serum sodium should call for a very guarded prognosis. By the time the extracellular fluid space becomes hypertonic, kidney function is markedly impaired, and it is the treatment of the underlying renal disease which becomes most important. If the underlying renal disease is reversible, prognosis is good. If it is not reversible, death usually follows.

CASE 4. C. P., a 77 year old white male, developed fever and chills 1 week before admission to the hospital. Two days later he noted swelling of the left shoulder with severe pain upon movement of the shoulder. He felt weak and developed anorexia. Physical examination on admission to the hospital revealed a well developed, fairly well nourished white male who appeared acutely and chronically ill. Examination of the eyes, ears, nose, and throat revealed nothing remarkable. Chest was clear to percussion, but there were occasional moist rales at the right base. The heart was normal in size, was regular at 120 per minute, the tones were good. Blood pressure was 104/60. Upon examination of the abdomen no abnormal condition was observed. There was a painful swelling of the left upper shoulder. The swelling was warm and the warmth extended to the left elbow and over the left pectoral muscle. Hemoglobin was 12½ grams, white blood count 14,800, bands 57, segmented 31, lymphocytes 3, monocytes 6, metamyelocytes 2, myelocytes 1. Urinalysis showed a 2 plus albumin, 4 plus sugar, many white blood cells per high power field. Fasting blood sugar was 490 milligrams per cent.

The patient was placed on 30 units of regular insulin, penicillin 200,000 units intravenously twice a day, and was given 2,500 cubic centimeters of 5 per cent glucose in water the first 2 days in the hospital. On the fourth hospital day the chloride was 104 milliequivalents per liter, bicarbonate 22 milliequivalents per liter, sodium 144 milliequivalents per liter, and the potassium 4.7 milliequivalents per liter. Needle aspiration of the left shoulder yielded 60 cubic centimeters of purulent material. This purulent material had a specific gravity 1.026, protein 6.4 milligrams per cent and was negative on culture for 48 hours.

On the fifth hospital day, the patient became increasingly lethargic, and studies on that day showed a fasting blood sugar of 111 milligrams per cent, nonprotein nitrogen 86.5 milligrams per cent, chloride 121 milliequivalents per liter, sodium 158 milliequivalents per liter, bicarbonate 24 milliequivalents per liter, and potassium 3.7 milliequivalents per liter. The freezing point of the serum was −0.67 degrees C. (360 milliosmols).

At this time it was noted that the patient had not been drinking, and in spite of the administration of 5 per cent glucose in water, it was thought that the low freezing point and the high serum sodium represented a primary water deficit. The patient was given 3 liters of 5 per cent glucose in water and 1 liter of normal saline intravenously and was encouraged to drink 1,500 to 2,000 cubic centimeters of water daily (Fig. 4). Serum sodium fell and the temperature which was elevated, returned to normal, and on the tenth hospital day the patient was alert and out of bed. Electrolyte studies on that day showed the blood sugar to be 212 milligrams per cent, nonprotein nitrogen 36 milligrams per cent, chloride 104 milliequivalents per liter, bicarbonate 23 milliequivalents per liter, sodium 136 milliequivalents per liter, and potassium 4 milliequivalents per liter. Freezing point returned to normal, −0.54 degrees (290 milliosmols) and the patient went on to make an uneventful recovery.

With large amounts of intravenous fluid used today, primary water loss in preoperative and postoperative states has become a rarity. In fact, it is primary water excess which is now the main problem. However, Case 4 demonstrates the significance of primary water loss with elevation of the serum

sodium and marked lowering of the serum freezing point demonstrating an excess of solute over water (Table I). Case 4 also shows rapid restitution of normal water and electrolyte balance following the administration of large amounts of electrolyte-free fluids orally and intravenously. The low freezing points in this case confirmed the high serum sodium and demonstrated primary water deficit in spite of what was considered an adequate intravenous fluid intake in the first days of hospitalization.

DISCUSSION

Significant deviation from the normal serum sodium level and normal freezing point depression is of grave concern to physicians and surgeons. A particularly perplexing situation arises in the postoperative patient receiving intravenous fluids who has a falling serum sodium level, decreasing urinary output, and occasionally a rising nonprotein nitrogen. The problem confronting the surgeon is whether the patient has a dilution hyponatremia from excess intake of fluids hypotonic to the serum as in Case 1, or a true salt depletion (decrease in total body sodium) as in Case 2, or a serious progressive underlying renal disease as in Case 3. The simultaneous comparison of the sodium level and freezing point depression of the patient's serum often points the way to the correct diagnosis and treatment.

Case 4 demonstrates the rising serum sodium and marked lowering of the freezing point of the serum in primary water loss. It is of interest to note that from a purely clinical point of view this patient was thought to have had an adequate intake of fluid during the first days which he spent in the hospital.

It is not that the level of the serum sodium or the freezing point depression of the serum in themselves is of great importance, but rather that these deviations from normal indicate a marked chemical disruption of the extracellular fluid compartment and are usually associated with serious illness. Applying the methods described a mortality rate of 67 per cent was found in the study of 70 hospitalized medical and surgical patients with abnormal serum sodium levels (Table III).

TABLE III.—STUDY OF 70 CASES OF ALTERATIONS OF THE SERUM SODIUM IN MEDICAL AND SURGICAL PATIENTS

	No.	*Died*	*Mortality, per cent*
Dilution hyponatremia	31	19	61
Sodium depletion	6	3	50
Hyponatremia with hyperosmolarity	22	18	82
Primary water loss	11	7	63
Total	70	47	67

It is not our purpose to suggest that the application of relationship between serum sodium and serum freezing point depression will ever substitute for a careful clinical evaluation of the patient. For example, there are a large number of chronically ill, usually elderly patients who normally have a low serum sodium level and an elevated freezing point of their serum. This is the so-called chronic cellular hypo-osmolarity "adaptation syndrome" or "tired cell syndrome." On the basis of serum sodium and freezing point depression these patients cannot be separated from patients with primary water excess. A serum sodium and freezing point depression prior to surgery and to intravenous fluid therapy will determine whether or not this syndrome exists. If this syndrome is present extreme caution should be used in fluid therapy in the preoperative and postoperative periods to prevent further fall in the serum sodium and serum tonicity by dilution with excess water.

The measurement of the serum freezing point should be looked upon as an adjunct to careful weighing of the patient, accurate checking of fluid intake and output, and serial electrolyte determinations in following a surgical patient in the preoperative and postoperative periods.

SUMMARY AND CONCLUSIONS

The combined use of serum sodium levels and serum freezing point depressions permits an accurate estimate of the state of water and electrolyte balance in the pre-

operative and postoperative state. Both determinations are relatively simple. The relationships between the two determinations aid in distinguishing four possible abnormal water and solute states namely: dilution (excess water), sodium depletion (true decrease in the body sodium), progressive renal disease, and primary water loss. An example of each type is given with suggestions for treatment.

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EXPERIENCES WITH 165 AORTIC HOMOGRAFTS

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HOMOLOGOUS AORTIC GRAFTS are now being widely employed for the purpose of replacing diseased segments of the aorta. Although sufficient time has not yet elapsed to permit any long term evaluation of the procedure in human beings, encouraging reports have appeared in the literature. The majority of these reports have dealt primarily with the indications for, and the early results of, this operation. Perhaps too little attention has been paid to problems directly related to the grafting procedure itself. It is our purpose in this article to comment on some of these problems. In addition, our method of collecting, storing, and preparing grafts for use will be reviewed briefly.

METHOD OF COLLECTING GRAFTS

The method of collecting and storing grafts at the Mayo Clinic has been reported previously by Mortensen and associates (6, 7). Briefly, the technique is as follows:

The homologous grafts are removed within 4 hours after death from suitable donors between the ages of 10 and 50 years. Donors are not considered acceptable when death was due to a virus or other transmissible disease, when widespread malignant disease is present, or when the exact cause of death is obscure. Unless evidence of atherosclerosis is noted, the entire thoracic and abdominal portions of the aorta and both common and external iliac arteries are removed under aseptic conditions; after débridement they are immediately placed in a storage medium containing Ringer's solution, human serum, and merthiolate. The graft is refrigerated at a temperature of from 2 to 4 degrees C. for 24 hours, after which time a specimen of the storage medium is removed for culture. The homografts are stored at from 2 to 4 degrees C. until used. At the end of 5 weeks, any unused vessel is discarded. A few of the earlier grafts were stored at −80 degrees C. in a dry ice and alcohol mixture which allows the arteries to be kept a longer time, but this procedure proved less practical than the present method and was abandoned. This technique is not to be necessarily a permanent one at our institution. At the present time, some grafts are being taken nonaseptically during routine necropsy and sterilized in a solution of beta propriolacetone. The use of freeze-dried grafts also is being anticipated.

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METHOD OF PREPARATION FOR USE

The technique of operation is essentially unchanged from that described in previous communications from this institution (2, 4). Immediately prior to use, an assistant prepares the homograft in the operating room under sterile conditions. Each branch is carefully inspected. If a branch has a tear at the point of origin, it is cut off flush with the side of the aorta and the defect is closed with No. 5–0 atraumatic arterial silk; otherwise the branch is ligated with No. 3–0 silk. When all branches have been secured, the graft is distended with saline solution under pressure and any further leaks are closed. The graft is now cut to the length needed to fit the patient and if a reasonable length of the graft remains, it is returned to the storage bottle and refrigerated for possible use at a later date. The graft is usually inserted with its posterior surface facing anteriorly in order that the lumbar or intercostal branches, which may leak when the clamps are removed, be readily accessible. The graft and the host artery are usually approximated end-to-end and anastomosis is accomplished

TABLE I.—AORTIC HOMOGRAFTS IN 165 CASES (MAY 1, 1953 TO JUNE 30, 1956, INCLUSIVE)

Diagnosis	*No. of cases*	*Deaths*	*Operative mortality rate, per cent*
Aneurysm of abdominal aorta	78	12	15.4
Occlusive disease of abdominal aorta	70	3	4.3
Coaretation of aorta	6	0	
Aneurysm of thoracic aorta	9	2	22.2
Superior vena caval syndrome	1	0	
Traumatic arteriovenous fistula	1	0	
Total	165	17	10.3

with running sutures of atraumatic arterial silk, No. 3–0 or No. 5–0 at the proximal end and No. 5–0 for the smaller distal vessels. In suitable cases, an anastomosis is made by the end-to-side technique, as described by Linton and Menendez.

REVIEW OF CLINICAL DATA

From May 1, 1953, until June 30, 1956, 164 patients underwent operation in which a segment of the aorta or of the common iliac vessels or of both was removed and an homologous aortic graft was inserted. In 1 additional case, the graft was used to replace a segment of the superior vena cava (Table I).

Aneurysms of the abdominal aorta. An abdominal aortic aneurysm was resected and replaced with a homograft in 78 patients. In 56 cases the aneurysm involved the aorta alone, while in the remaining 22, one or both common iliac arteries also were involved. In 4 cases rupture of the aneurysm had occurred before operation. A thoracic graft was used to bridge the defect after the method of Dubost in 65 cases, but in 13 the disproportion in caliber between the host aorta and the graft was not so marked and continuity was re-established with a bifurcation graft.

Of the 78 patients who underwent operation 12 died while in the hospital, an operative mortality rate of 15.4 per cent among the patients with aneurysm. In 4 cases, death occurred some time after the patient's dismissal from the hospital, resulting in a late mortality rate of 6.1 per cent of the survivals. In 74 cases, the operation was elective and 11 of the 12 hospital deaths occurred among patients in this group. Of the 4 patients in whom rupture of the aneurysm had occurred necessitating emergency operation, 1 died in the hospital.

Of the 12 patients who died in the hospital 5 died in the first week, 2 in the second week, 4 in the third week, and 1 in the fifth week. The 4 patients who died after leaving the hospital died 6 weeks and 13, 16, and 18 months after operation, respectively.

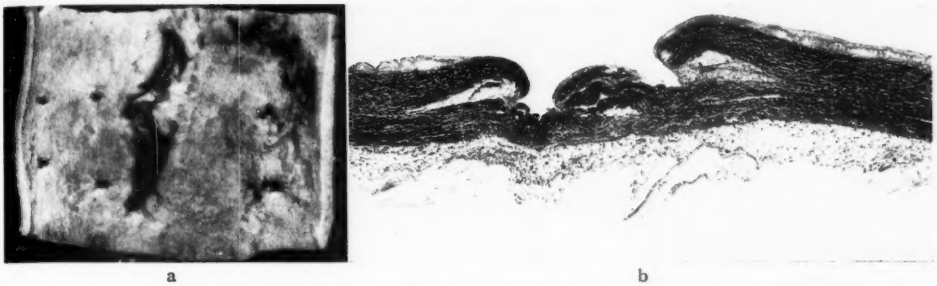
In evaluating the causes of death it became apparent that the deaths could be grouped into two categories as follows: (1) deaths related to the graft itself and (2) deaths not related to the graft. Seven of the 16 deaths among patients operated on for aneurysms resulted from rupture of the graft or hemorrhage from the suture line and observations concerning these 7 are presented in a separate section of this paper. Among the 9 patients dying from causes not related to the graft, lower nephron necrosis with uremia occurred in 2 patients. One died on the seventh and the other on the eighteenth postoperative day.

Gangrene of the intestine was responsible for 2 deaths. In 1 patient postoperative thrombosis of the superior mesenteric artery occluded the blood supply to the entire bowel and resulted in gangrene of the small and large intestines. The second patient died of gangrene of the left portion of the colon following ligation of the inferior mesenteric artery at the time of operation.

One death resulted from a large mural thrombus that developed immediately above the homograft, occluded the orifice of the right renal artery, and produced massive infarction of the right kidney with uremia. At necropsy this patient also was found to have had acute pancreatitis.

Acute myocardial infarction caused death in 2 patients; 1 died during the third postoperative week and 1, 13 months after operation. Pulmonary embolism accounted for 1 fatality.

The last patient died 18 months after operation following rupture of an aneurysm of the left internal iliac artery. At the time of



a b

FIG. 1. Abdominal aortic aneurysm in a 71 year old man. After placement of a homologous aortic graft, rupture of the graft occurred on the eighth postoperative day. At a second operation, the ruptured segment was removed and the bridge in the first graft filled with a second graft. Death occurred 26 days after the second operation from rupture of the original graft at the site of suture. a, The resected portion of the first graft. Hemorrhage occurred through a linear rupture of the aorta. Note the openings of two pairs of intercostal arteries on the left side of the illustration. b, Portion of first graft which was not removed at the second operation. This segment had cystic medial necrosis and several foci of disruption of the media and intima, one area of which is illustrated in the photomicrograph. This lesion is a miniature of the large rupture shown in "a"(Verhoeff's elastic tissue stain, counterstained with van Gieson's connective tissue stain, ×13).

operative removal of the abdominal aortic aneurysm, the left internal iliac artery was found to be dilated but not aneurysmal.

Arterial thrombosis occurred in 3 patients during the early postoperative period. In 2 patients it was unilateral and resulted in claudication in the affected leg. The third patient suffered bilateral femoral thrombosis with subsequent claudication in both legs.

Occlusive disease of the abdominal aorta. Resection and replacement with a homologous aortic graft for occlusive disease were performed in 70 patients (Table I). The occlusive process was usually extensive, requiring a bifurcation graft and in only 14 cases was a localized procedure deemed adequate. The early functional results in some of these cases have been reported (9).

Three deaths occurred in this group of 70 patients, a mortality rate of 4.3 per cent. One patient died several hours after operation following hemorrhage from the upper anastomosis. The second death occurred on the tenth postoperative day from lower nephron nephrosis and uremia following a period of hypotension on the second day after operation. The third patient was reexplored on the third postoperative day because of rupture of the graft at its bifurcation. The ruptured graft was removed and replaced with a second "Y" graft. Lower nephron nephrosis with oliguria developed, however, and the patient died on the tenth day after operation.

Unilateral arterial thrombosis developed in 6 patients after operation. Two patients subsequently required amputation of the involved leg. The other 4 patients had symptoms of claudication in the ischemic extremity.

Coarctation of the aorta. In 6 patients, 4 of whom were adults, a homograft was used to replace a coarcted segment of the aorta (Table I). In 3 patients, conditions were typical in most respects but the length of the coarctation prevented direct anastomosis. A fourth patient had a large, saccular aneurysm just distal to the coarctation.

Another patient had a rather marked degree of aortic regurgitation. At operation the long segment of narrowed aorta was resected and a graft was sutured to the aorta at the upper line of resection. The distal end of the graft was attached to the upper end of a Hufnagel valve while the lower end of the artificial valve was attached to the patient's descending aorta. In the last case, that of an 18 month old girl, the coarctation was lo-

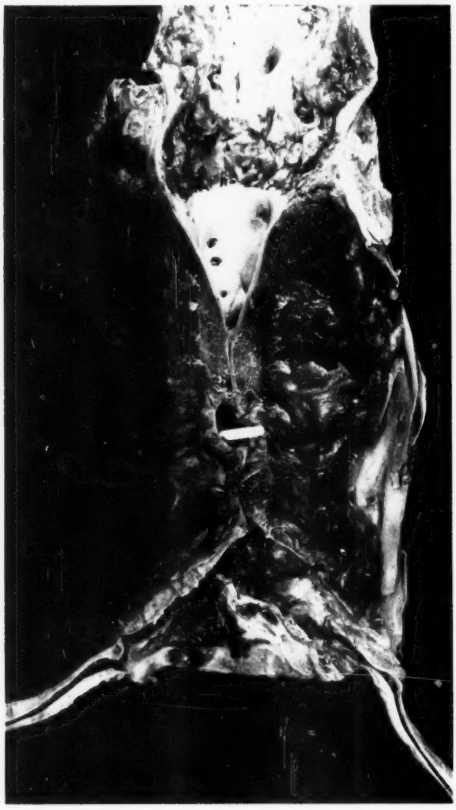


FIG. 2. Abdominal aortic aneurysm in a 59 year old man. Posterior view shows abdominal aorta and iliac vessels with homologous aortic graft. The probe lies in a perforation of the posterior aspect of the graft which led to a fatal hemorrhage 39 days after placement of the graft. Retroperitoneal hematoma lies to the right of the graft and between the aorta and inferior vena cava.

cated at the junction of the thoracic and abdominal portions of the aorta. Each of the 6 patients survived and has a satisfactory result.

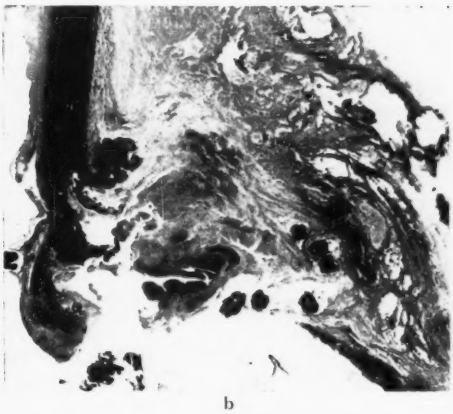
Aneurysms of the thoracic aorta. In each of 4 patients with an aneurysm of the descending thoracic aorta and in 5 patients with an aneurysm of the distal aortic arch, resection of the involved segment of aorta was followed by placement of an homologous graft (Table I). Four of the 9 aneurysms were due to atherosclerosis and 2 were due to congenital defects; 1 was associated with a dissecting aortic aneurysm, and 1 aneurysm was of syphilitic origin and 1 was of traumatic origin.

Two deaths occurred in this group of 9 patients. In the patient with a dissecting aortic aneurysm, an attempt was made to resect a saccular aneurysm at the junction of the distal aortic arch and thoracic aorta and to replace the segment with a homograft. A temporary shunt was used to bypass the aneurysm during resection. Death followed hemorrhage from the site of the proximal connection to the aorta. The second death occurred in a patient with a saccular aneurysm of the lower thoracic aorta that had perforated into the esophagus. Thirty-one days subsequent to resection and insertion of a homograft, this patient had massive hemoptysis and died. At necropsy a separation of the homograft and the host aorta was found at the site of the lower anastomosis.

Superior vena caval syndrome. One patient with obstruction of the superior vena cava secondary to fibrous mediastinitis underwent resection of the superior vena cava and insertion of an aortic homograft. Five months later symptoms recurred. A second operation was performed. Marked reaction was noted in the fibrous tissue surrounding the graft and constriction had developed. The obstruction was relieved by the insertion of a wide ivalon prosthesis between the left innominate vein and the right atrium. This patient is alive and well at the time of this writing.

Arteriovenous fistula. One young patient gave a history of rapidly progressive congestive heart failure which developed immediately after surgical removal elsewhere of a protruded intervertebral disk. He was found to have a large fistula between the right common iliac artery and the inferior vena cava which was corrected by resecting the terminal aorta and the right common iliac artery, closing the inferior vena cava and inserting a homograft to bridge the site of aortic-iliac resection.

a



b

FIG. 3. a and b, Abdominal aortic aneurysm in a 55 year old man. a, The illustration from behind shows the aorta and the graft which had been placed 16 months previously. A rupture in the right side of the graft (edge of rupture in rectangle) led to a false aneurysm (*A*) to the right and in front of the aorta. The false aneurysm in turn ruptured into the duodenum (*D*) leading to fatal intestinal hemorrhage. The communication between the false aneurysm and the duodenum is not shown in this illustration, since it lay more anteriorly than this perspective. b, Mural thrombus present in graft. Edge of rupture of aorta and of adjacent false aneurysm (area in rectangle in *A*). The aortic wall shows a sudden interruption in continuity. The false aneurysm lies to the right in the illustration (Verhoeff's elastic tissue stain, counterstained with van Gieson's connective tissue stain, ×9).

GRAFT FAILURES

In the entire series of 165 cases there were 10 deaths (6 per cent) related directly to some failure in the grafting procedure, either rupture of the graft or hemorrhage from the suture line. Seven deaths occurred early in the postoperative period; the other 3 occurred much later. Eight of these 10 deaths occurred in patients operated on for aneurysms.

Necropsy was carried out in 9 of the 10 cases. Particular study was made of the homograft and adjacent segments of the host aorta. Hematoxylin and eosin stain and elastic tissue stain were used and the histologic appearance of these vessels was compared with the appearance of the same vessels in the cases in which death had resulted from other causes.

In 3 patients definite evidence showed that the graft itself had failed. In each of these 3 cases a break had occurred in the continuity of some part of the graft.

In only 1 instance was there histologic proof that the graft was defective. This graft ruptured in its midportion on the eighth postoperative day (Fig. 1a) and was partially resected and replaced with a second homologous graft. Three weeks later a second and fatal rupture occurred through a hole in the original graft where a stitch had been placed at the time of the second operation. Microscopically, patchy areas of cystic medial necrosis were present throughout the original

FIG. 4. Abdominal aortic aneurysm in a 67 year old man who died on the fifth postoperative day of hemorrhage from the upper suture line. Junction of patient's aorta with upper end of homologous graft is shown. Above the point of the arrow, a triangular-shaped defect extends into the graft from the suture line. A possible cause for this break may lie in the disproportion in size between the wide aorta of the patient and the normal size of the graft.

graft and overlying one of these the intima and underlying media were broken, with dissection by blood for a short distance into the media (Fig. 1b). The other two grafts in this group did not show histologic changes which differed from grafts available for study in patients dying of other causes.

One of these grafts which ruptured in its midportion 6 weeks after operation is shown in Figure 2. One can only postulate that rupture might have occurred at the origin of a ligated vessel or at the site of a small unrecognized atherosclerotic plaque. One patient in this group died 16 months after operation. Rupture of the graft had occurred through the anterior wall and the resultant hemorrhage formed a retroperitoneal false aneurysm which in turn ruptured into the duodenum (Fig. 3a and b). In the series reported by Humphries and associates, 3 postoperative deaths resulted from hemorrhage into the duodenum or jejunum.

Histologically, the grafts in the 6 patients dying of hemorrhage from the suture line were no different from the grafts in patients dying of other causes. In these 6 patients death may have been due to either a graft failure or a technical error. Histologic study failed to help in clarifying this point.

Quite probably the disproportion in diameter of the lumen which frequently exists between the host aorta and the graft plays a part in disruption of a suture line (Fig. 4). This might help to explain the higher incidence of disruption of the suture line after resection of an aneurysm than after resection of an aortic occlusion. Excessive disproportion is not infrequent in cases of abdominal aortic aneurysm. In many cases advanced atherosclerosis is present in the host vessels; consequently they do not hold sutures firmly and the anastomoses are, at best, insecure. This condition undoubtedly contributes to the hazards of suture-line separation.

In the present series 1 patient underwent 3 operations after the original graft had been inserted. The first was necessary to repair a disrupted anastomosis; re-exploration revealed a rupture of the graft which was resected and replaced with a second homograft. Four days later it was again necessary to operate and close a separated suture line, and the patient died 21 days after the original operation. The experiences in this case lead us to mention the report of Nyhus and associates. They postulated, after observing degeneration of homografts in experimental animals, that an immune reaction between the host and the homograft, which they considered to be weakly antigenic, might be a factor in the degenerative process. As yet, however, we do not have objective proof that such a reaction occurs.

Thrombosis of the graft or the adjacent host arteries or both occurred in 9 patients after operation. This complication was seen twice as often after operations for occlusive disease as after resection and grafting of abdominal aortic aneurysms. It is likely related to the inadequate runoff for the increased flow of blood through the grafted aorta in patients with extensive occlusive disease rather than to defects in the graft per se, although such defects and also technical errors may play a part in some cases.

SUMMARY

Clinical experiences with 165 aortic homografts have been presented with particular emphasis on problems directly related to the grafting procedure itself.

There were 17 deaths in the 165 cases. In 10 patients death was considered due to "failure of the graft." Necropsy was performed on 9 of the 10 patients. In 3 of these the graft had ruptured, and in the other 6 patients death resulted from hemorrhage originating at the suture line. In these cases this complication might have been due either to intrinsic weakness of the graft or to a technical error.

Several factors may contribute to failure of the graft. Intrinsic disease of the graft itself was present in 1 instance. Disproportion in size between the remaining host aorta and the graft probably accounts for some failures. The poor quality of the host aorta in some cases may be a contributory factor. An immune reaction to the foreign graft may also play a contributory role.

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OBSERVATIONS UPON THE EXPERIMENTAL REPAIR OF THE TRACHEA USING AUTOGENOUS AORTA AND POLYETHYLENE TUBES

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DESPITE THE RELATIVE PAUCITY of clinical cases, recent interest in the use of polyethylene tubes as implants to recreate the continuity of the resected trachea or to re-establish the adequacy of a stenosed lumen has been very great. A variety of methods and many other substances have been used to accomplish this, but polyethylene prosthetic tubal implants, particularly for full circle defects, apparently remain the method of choice.

This report of the general principles involved is based upon surgical experiments performed on 123 dogs in attempts to repair large defects of the cervical trachea and to recreate the airway after total circumferential excisions up to 10 rings in length.

From an anatomic standpoint, the trachea is a single organ, but environmental differences between the cervical and thoracic portions create entirely different problems insofar as surgical repair of the two segments is concerned. Experiences limited to the cervical trachea can by no means be taken for granted as applying to the thoracic portion and vice versa. Although certain facts remain common to the two, the muscular surroundings of the cervical trachea and the close adaptation of other tissues to it present advantages of tissue support and blood supply not enjoyed by the thoracic segment.

If a relatively small fenestra-type defect of a centimeter or two is created in the trachea, granulation tissue will fill the defect, it will become epithelialized on the inner surface, and healing by fibrosis will rapidly occur. This is commonly seen in the everyday healing of tracheotomy wounds.

If the fenestra is large, granulation tissue, which may be obstructive, will grow within the fenestra before the epithelialization can be completed. To prevent this a covering is required for all large tracheal defects. Fascia lata or other heavy fascia has been successfully used by Jackson and associates with rapid replacement by the fibroblasts of the host and epithelialization of the luminal surface. Other materials serve as well, and we have successfully employed decalcified homologous bone in sheets (scapulae, or split hollowed-out femurs) and preserved dura mater. Particularly noteworthy is the use of lyophilized homologous aorta which, in almost every case, can be depended upon to result in successful closure of large defects up to 10 rings in length and half the circumference of the trachea or more. These implants survive as aortic tissue for many months, retaining their elastic tissue elements in a pattern closely approximating the normal often for periods as long as 2 years. The margins of the homograft become intimately blended by fibrosis to the cut edges of the tracheal fenestra. By serving as a framework the aortic homograft greatly enhances the speed of the healing processes about the tube and epithelialization within it.

The intimal surface of such aortic implants heals with an epithelial surface comparable to that of tracheal epithelium. Contraction of the fibrotic aorta narrows the defect by pulling the severed ends of the trachea together. Because of the contracture,

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the use of polyethylene or tygon tube as a combined stent and airway is essential if the defect is sufficiently large.

There is no single instance reported of successful replacement of full circumference tracheal segments created solely from the tissue of the host, or from homologous transplants unaided by the presence of rigid or semirigid prosthetic devices. Isolated instances of clinical success have been described following the use of tantalum or stainless steel wire or mesh or inert tubing surrounded by fascia or skin. Similar attempts on our part to repeat the success of others have invariably failed. Experiments upon the large series of dogs herein reported have convinced us that there is currently no better method for re-establishing continuity following resection of an entire segment of cervical trachea than the successful technique originally used by Longmire in a young patient following evulsion of essentially the entire segment of cervical trachea. Longmire inserted a polyethylene tube into the defect, and it remained *in situ* for 11 years. Ten and one-half months postoperatively, an unsuccessful attempt was made to remove the polyethylene prosthesis. Although an epithelium-lined tube had formed about it, there was not sufficient rigidity of its wall to permit adequate inspiration without collapse of the pseudotrachea nor could the ends of the tracheal segments be approximated. The tube has recently been successfully removed and the severed ends of the trachea sutured end to end. The healing process by which this became possible is that of "tracheal stretching," the result of contraction of the fibrous tissue cuff which had formed about the polyethylene tube. This phenomenon which has not previously been reported will be described in subsequent paragraphs.

Polyethylene as a tracheal prosthetic insert enjoys many advantages. Grindlay and Mann describe its chemical similarity to paraffin and point out that it is not wetted by water. There is, therefore, no tendency for secretions to adhere to it, and many instances are given of its use without any tendency toward obstruction from bronchial mucus or other secretions which do not adhere to its surface. This is not true of metals or glass tubes in which mucus does tend to adhere and become obstructive. Not all investigators agree, however, that the polyethylene serves adequately as an escape route for retained secretions, and some believe that the loss of normal ciliary activity is the cause of the high incidence of pulmonary sepsis which they encountered. The material is sterilized by boiling in water for 20 minutes, or by washing in ether or alcohol mixtures followed by immersion in 1:1000 aqueous zephiran for ½ hour. Sutures are relatively easily placed through it so that it can be fixed *in situ*.

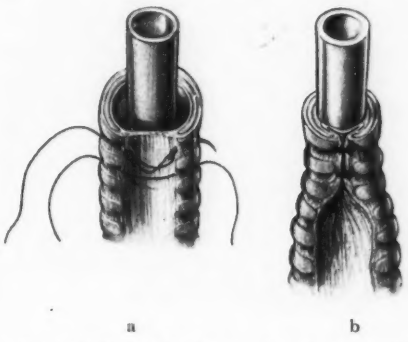

FIG. 1. Method of cinching trachea about polyethylene tubal prosthetic stent.

There seems to be very little to gain from the use of individually prepared and wrapped polyethylene tubes rather than the commercially prepared variety, but when it is considered advantageous to do so, molded forms can be made after the method described by Grindlay and Mann.

Studies to ascertain the end result of Longmire's technique by long term observations upon dogs have been carried out. The diameter of the tubes selected for use in the dog depended, of course, upon the size of the dog and the diameter of its trachea. In the experiments herein described, the tubes used had an internal diameter of 1.4 centimeters

and a wall 2 millimeters thick. These agree roughly with the sizes used by Swift, Grindlay, and Clagett. If the trachea was too large in diameter to fit snugly around the polyethylene insert, the latter was "cinched" by a Lembert suture placed through the membranous trachea—one placed at the upper and one at the lower end of the tracheal stump—and drawn taut (Fig. 1).

The method of adapting the tube to the ends of the trachea is of great importance. Several factors are concerned: chiefly, the tracheal blood supply, which will be described. Suturing the insert to the trachea by an end-to-end technique has invariably failed not only because of the "hinge effect" following the use of full circumferential homografts to replace totally excised segments as described by Jackson and associates but because separation of the suture line occurred from the very forceful pull produced by the invariable initial retraction of the lower segment into the thorax.

The method employed for insertion of the polyethylene tube into the tracheal defect needs, therefore, to be that of a "sleeve" insertion; the implant is telescoped into the lumen of the trachea for a distance of about 2 rings at each end. The polyethylene tube must always be telescoped into the trachea and never the reverse. While the diameter of the tubes used in our experiments (8) does not in any case permit telescoping the tracheal stump into the tube, nevertheless, there are experiments reported by others in which tubes large enough to permit this have been used. These have invariably resulted in separation by sloughing with loss of the prosthetic implant. This failure is due to the very peculiar blood supply of the cartilaginous tracheal rings, the details of which are of great practical importance.

Blood is supplied to the trachea of the dog from two sources; the first source supplies the posterior aspect, chiefly the membranous trachea, and the second supplies the anterior two-thirds of the circumference comprising the tracheal cartilaginous rings. Pacheco, Rivero, and Porter have likewise alluded to this in their studies at the University of Mexico. The rings are segmental, each pair having an essentially independent supply of blood from vessels passing horizontal to it. If an intercommunication between these vessels does exist, it is inadequate to nourish adjacent rings when they are isolated by being telescoped within an encircling cuff. Photographic illustrations of this have previously been published by Pressman. In addition to these disadvantages occasioned by the peculiarities of the blood supply to the rings, Morfit and associates reported that telescoping the trachea into the lumen of the prosthesis promotes stricture formation and enhances the likelihood of the occurrence of occluding granulomas.

In reversing the procedure and telescoping the implant into the trachea, the temptation to flange the ends of the implants and to place an encircling suture below the flanged segment as an encircling stay is unsatisfactory because of the strong possibility that the encircling suture will slough through the wall of the hollow organ, coming to rest about the prosthesis itself. Daniel and his co-workers, for instance, found this true in 14 out of 14 cases; other investigators have had the same experience. With respect to the trachea, this possibility represents an especially dangerous hazard, since the polyethylene implant then lies free within the tracheal lumen and is apt to be displaced downward. Often it comes to lie in an oblique plane or to impinge on the carina, thus producing respiratory obstruction. This complication has been demonstrated experimentally and has also been described as a fatal clinical occurrence. If the displaced tube does in itself occlude respiration, then the flaccid fibrous tube which has formed around it collapses sufficiently to prevent adequate inspiration. The method of fixation of the polyethylene implant within the lumen of the trachea is, therefore, of great practical importance and requires careful attention.

Fixation of the tube in place is best accomplished by metal through-and-through sutures with no advantages demonstrable

between stainless steel, vitallium, or tantalum. In the early instances of the use of metal sutures, some difficulty was encountered by reason of the mechanics inherent in passing the bight of the threaded metal suture through the firm wall of the polyethylene implant. Accurate placement of these metal sutures can be greatly simplified by using a 1½ inch, No. 18 gauge hypodermic needle which is inserted in a through-and-through manner to include the muscles of both sides, the tracheal wall, and the implant. The metal suture is then placed through it, as if the latter were a stylet. The lumen of the needle is entered at its point rather than at the hub. This is more easily accomplished if the bevel of the needle is turned upward in plain view of the operator. The needle is withdrawn and the metal suture is left in place. The ends are then fixed with hemostats until ready to be fixed over a button on the outside of the skin or tied and buried. By this technique, relatively heavy sutures can be used without any apparent disadvantage. They have, in our experience, remained *in situ* for as long as 18 months without impeding the expectoration of mucus or pus-producing obstruction from retained debris, or permitting slippage of the tube. When removed after this time, the tubes sometimes present a deposit of thin sediment, the source of which is unknown, but which has never been found to be harmful or excessive in amount. There has been no instance in which the tube has failed to remain patent.

The length of the tube is important and can easily be misjudged. If too long and impinging above upon the structure of the larynx, it will invariably produce obstructive granulomas. If the tube is too long inferiorly it can impinge upon the lumen of the esophagus at the level of the thoracic inlet, narrowing it sufficiently to cause obstructive dysphagia. In early experiments upon dogs, this phenomenon resulted in many casualties from inanition and starvation. This mishap has not occurred since steps were taken to prevent the tube from entering the thoracic inlet. The possibility of error in estimating the proper length of the tube, due to the position of the animal's head and neck should not be overlooked. During the operation, the head is ordinarily extended and stretched far back to make the structures of the neck more prominent with resulting elongation of the trachea. When the animal's head regains the normal position of semiflexion, a prosthesis, which at the time of surgery had extended for a proper distance above and below the cut ends, respectively, will have become too long. Prostheses should, therefore, be cut to proper size with the head of the animal semiflexed.

The problem of obstructive granuloma formation at the ends of the polyethylene tubes was a serious handicap in the earliest of our experiments and occurred in virtually every animal after 2 weeks to 4 months, regardless of whether the tube ends were sharp or smoothened or the tube tapered or not. This has been greatly lessened by the use of the aortic homograft as a patch over the tracheal defect. Apparently, the homograft prevents the invasion of granulomatous tissue from the area immediately surrounding the tracheal defect and from the cut raw ends of the tracheal margins as well. A definite relationship between the granuloma formation and a piston-like movement of the prosthesis within the trachea apparently exists. Hence, the tube needs to be firmly fixed within the trachea, so that the insert will ride up and down with it and take part in its lateral movements as well. No granulations have formed serious enough to obstruct the airway since the use of 2 wire sutures to fix the prosthesis to the trachea was instituted routinely. This technique is, therefore, of considerable practical importance. When the lower suture is omitted, so that a "riding up" of the lower segment of the trachea over the lower end of the tube takes place, the incidence and severity of granuloma formation is increased. Morfit and associates cite granuloma formation as the most frequent cause of failure and give 6 causes as follows: (1) cut tracheal ends telescoping the trachea into the tube; (2) growth through permeable

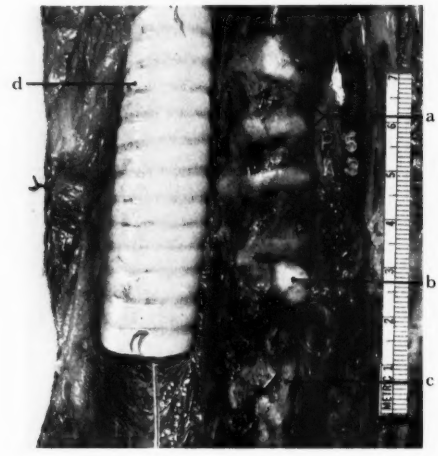

FIG. 2. Elongation of trachea from stretching of interspaces 2 years postoperatively following resection of 10 rings of trachea and replacement with homologous aorta. *a*, Stretched membrane between adjacent tracheal rings; *b*, small cyst not connected with experiment; *c*, site of resected segment and membranous pseudotrachea formed about polyethylene tube; *d*, normal trachea.

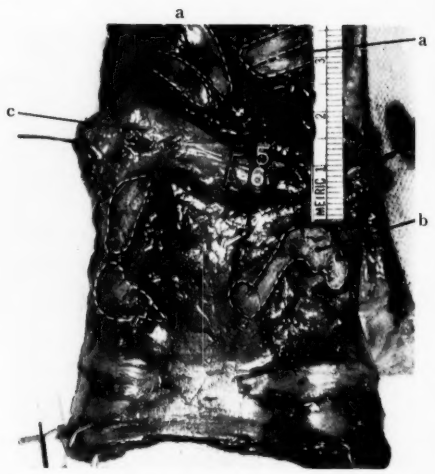

FIG. 3. Posterior view of trachea split anteriorly demonstrating distortion and calcification of tracheal rings above and below aortic implant (2 years after operation). *a*, Distorted tracheal rings; *b*, calcified tracheal ring below membranous pseudotrachea with greatly widened membranous interspace below; *c*, site of resection of trachea with formation of membranous pseudotrachea.

stents; (3) too great a length of prosthetic tube; (4) narrowing of the diameter of the inlaying prosthetic tube with the ingrowth of granulomas through the gap; (5) breaking of suture with the ingrowth of granulomas at the point of separation; (6) too great a tension resulting from sutures tearing through.

When a length of polyethylene tubing is properly inserted into a tracheal defect, a flaccid collapsible fibrous tube will rapidly form about it in a matter of weeks; the fibrous tissue arises from the surrounding soft tissue bed. In a matter of months, this fibrous tube eventually becomes epithelialized with respiratory epithelium by a growth of mucosal cells from above and below. The length of time during which this takes place, as well as the length of dehiscence to be covered, varies tremendously with many unknown factors. At first, the mucosa is thin and nonciliated, but it eventually becomes stratified, columnar, and ciliated. In cases of complete resection of the cervical trachea, this ultimate result has required more than a year.

TRACHEAL STRETCHING

Having formed about the polythelene implant, the membranous pseudotrachea eventually contracts, molding itself tightly to the contour of the tube. Experiments are currently being undertaken to determine the length of time during which such contracture will continue. Although they are not yet sufficiently advanced to make a positive statement, continued contraction and fibrous tissue activity has been noticeable for a period longer than 8 months. The contraction is not only circumferential, but vertical as well, causing a gradual stretching of the remaining tracheal segments above and below the site of resection. This results from a widening of the intercartilaginous membrane between the rings to as much as 15 times normal width (Fig. 2). Stretching and widening of the membranous rings take place in the remaining tracheal segments, both proximal and distal to the fibrous segment which bridged the defect.

Figure 3 presents an observation of added interest. Immediately to the left of the rule,

at the 2 centimeter mark, is a double, hook-like prominence. This is the first tracheal ring below the excised segment. It has been pulled upward for a distance of 2 centimeters, distorted in shape, and angulated by the forces of fibrous tissue contraction; it is of great interest to note that this ring has become densely calcified, whereas no calcification is evident in any of the rings found in their normal position. Calcification and actual ossification of the stretched and often distorted tracheal rings have been frequently observed in the experiments herein reported. It is considered to be a reaction of injury due to disturbances of the blood supply. This phenomenon will be described subsequently.

While Clagett, Grindlay, and Moersch make no special point of it, they have reported closure of a fibrous tissue gap, which measured 2.5 centimeters at the time of operation, to a length of only 1 centimeter, 2½ months postoperatively. Likewise, Daniel, Taliaferro, and Schaffarzick refer indirectly to the same phenomenon. One could hopefully expect that this fibrous pseudotrachea might eventually become sufficiently firm and rigid to permit the ultimate removal of the prosthesis without tracheal collapse. Such a fortunate outcome has, however, not been reported. The pseudotrachea remains a flaccid tube which is drawn in with each respiratory effort. Even in short segments of 1 to 2 centimeters, this movement is sufficient to occlude respiration and require the continued presence of a permanent indwelling supportive prosthesis.

SUMMARY AND CONCLUSIONS

Resections of the complete circumference of the cervical trachea of such length as to make end-to-end suture impossible require an indwelling prosthesis to bridge the defect. The most satisfactory material from which to make such a prosthesis seems to be polyethylene (or tygon) tubing. Because of the distribution of blood vessels to the tracheal rings, this prosthesis must be telescoped into the lumen of the tracheal segments rather than vice versa. When so inserted, the tubing has a tendency to be displaced downward and to occlude respiration. This mishap may occur at any time for many months postoperatively. In large measure, however, it can be avoided by using stainless steel wire fixation sutures, No. 24 gauge or heavier, placed through the muscles of the neck, the residual tracheal wall, and the polyethylene tube, and drawn out of the muscles on the opposite side. The sutures must then be tied or twisted across the midline and buried or fastened to buttons externally. The use of such a prosthesis requires careful planning to avoid too long a tube, the result of which may be the formation of occluding granulomas at the laryngeal level or interference with swallowing at the thoracic inlet.

The occurrence of granulations at either end of the prosthesis is stimulated by any untoward degree of movement of the tube. It is lessened by proper fixation of the tube and the use of an aortic homograft as a patch closing the defect. A fibrous pseudotrachea forms, which ultimately epithelializes throughout its luminal surface. It undergoes contraction in a circumferential and longitudinal direction of such magnitude as appreciably to stretch the remaining segments of the trachea above and below the defect. The tube thus formed never gains a sufficient degree of rigidity to remain patent during inspiration. This latter shortcoming necessitates the continued presence of an indwelling polyethylene prosthesis, but there is evidence at hand to indicate that contraction of the fibrous tube that forms about the polyethylene may be of sufficient magnitude to permit, in some cases and after a period of years, an end-to-end anastomosis of the upper and lower tracheal segments, whereas this was not possible initially. This result is produced by the stretching of the membranous rings. There is some disagreement as to whether or not the polyethylene tube, because of the absence of normal cilia, hinders the escape of pulmonary and bronchial secretions, but it is generally agreed that polyethylene is less objectionable in this respect than metallic tube inserts.

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ARTERIOGRAPHY OF THE UPPER EXTREMITY

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WILLIAM E. ALLEN, JR., M.D., St. Louis, Missouri

ALTHOUGH ARTERIOGRAPHIC DEMONSTRATION of the vessels within the lower extremity has been found to be safe and useful, similar examination of the arteries of the arm has been somewhat limited in its application because of the greater frequency and severity of complications attending it. However, during the past 18 months the percutaneous injection of the subclavian artery with sodium diprotrizoate[1] has been found to be a convenient and safe method for the roentgenologic demonstration of the arteries of the upper extremity in 19 cases. This method has proved to be useful in determining the patency of arterial anastomoses and in evaluating the pattern and the extent of occlusive arterial disease in the upper extremity.

TECHNIQUE

The technique consists of the supraclavicular percutaneous injection of sodium diprotrizoate into the subclavian artery where it crosses the first rib (Fig. 1). The only contraindication is hypersensitivity to the medium. A test dose of 1 cubic centimeter is given intravenously before the examination.

The intracutaneous and periarterial injection of 1 per cent procaine usually provides sufficient anesthesia and only once was general anesthesia necessary for an apprehensive patient. Preliminary stellate ganglion block is now considered unnecessary. The skin wheal is raised just above the clavicle where the pulse in the subclavian artery is palpable. This point is usually 1 to 3 centimeters medial to the midpoint of the clavicle when the shoulder is depressed, and is slightly medial to the lowest visible part of the distended external jugular vein. The arm is slightly abducted, and the position of the forearm is selected according to the purpose of the examination. The radial and ulnar arteries are not obscured by bony shadows when the forearm is rotated 90 degrees. The palmar arch and digital vessels are best visualized with the hand pronated (Fig. 2) or supine. When the hand is supine, however, the distal brachial artery is covered by the shadow of the lower humerus.

The Cournand needle, size 20 or larger, is inserted through the anesthetized skin perpendicular to the clavicle to a depth of about 3 centimeters. The pulse in the subclavian artery may be palpated through the skin or with the tip of the advancing needle. The occurrence of brachial plexus paresthesias indicates that the needle is too far lateralward. If the needle tip encounters the first rib without meeting the artery it should be introduced more laterally, or the needle tip may be "walked" along the rib laterally until it encounters the artery. Then the needle tip is advanced through the arterial wall, and the stylet is withdrawn. The needle hub is directed 45 to 60 degrees medially and posteriorly and the needle tip is advanced 1 to 2 centimeters farther within the lumen of the artery. The patient is warned about the momentary burning sensation and cautioned to hold perfectly still. The syringe is connected to the needle and the arteriogram is performed by the injection of 20 to 30 cubic centimeters of 30 per cent sodium diprotrizoate in 10 seconds or less. Toward the end of the injection, the first film is exposed. Films can be changed every 1 to 3

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[1]Sodium 3,5-bispropionamido 2,4,6 triiodobenzoate—trade-name, miokon.

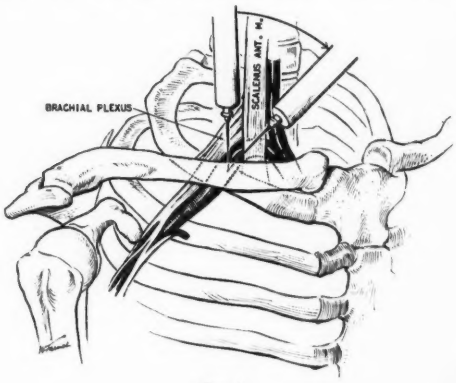

FIG. 1.

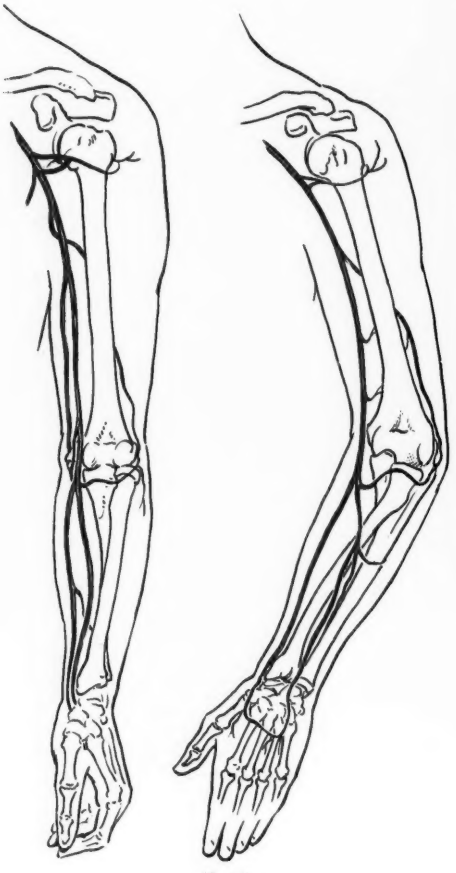

FIG. 2.

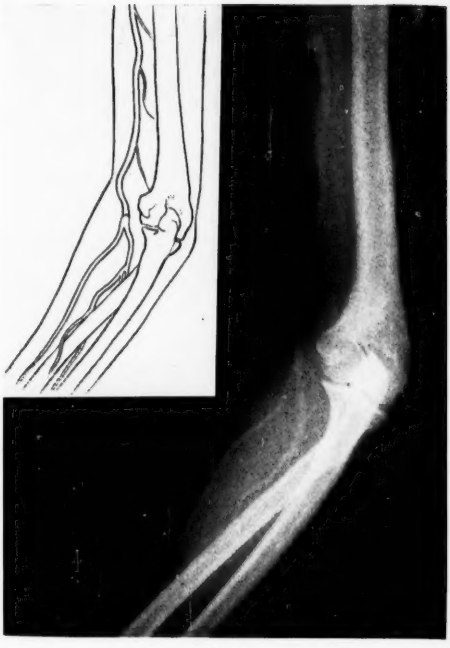

FIG. 3.

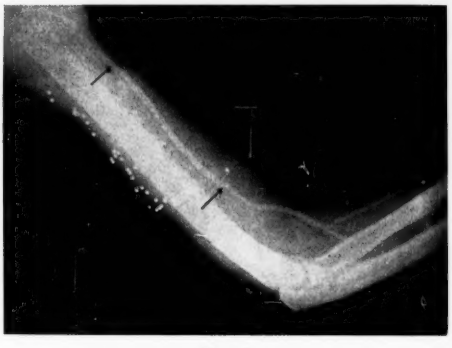

FIG. 4.

FIG. 1. Relations of the subclavian artery.
FIG. 2. The arteries in various positions of the arm.
FIG. 3. End-to-end anastomosis of distal brachial artery.
FIG. 4. End-to-end brachial artery homograft (1).

seconds by hand, or more frequently by the use of the Sanchez-Perez changer. Serial films are particularly helpful for arteriovenous fistulas in which the circulation time

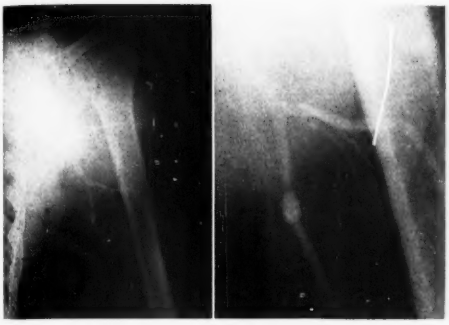

FIG. 5.

FIG. 6.

FIG. 5. Stenosis of anastomosis and poststenotic dilatation of the brachial artery.

FIG. 6. Thrombosis of the axillary artery.

FIG. 7. Thrombosis of the distal brachial artery with partial recanalization.

FIG. 8. Brachial arteriovenous fistula.

is more rapid and for cases of occlusive disease in which the circulation time is slowed.

RESULTS

The indications for and results of the arteriograms are summarized in Table I. Postoperative arteriograms were performed

FIG. 7.

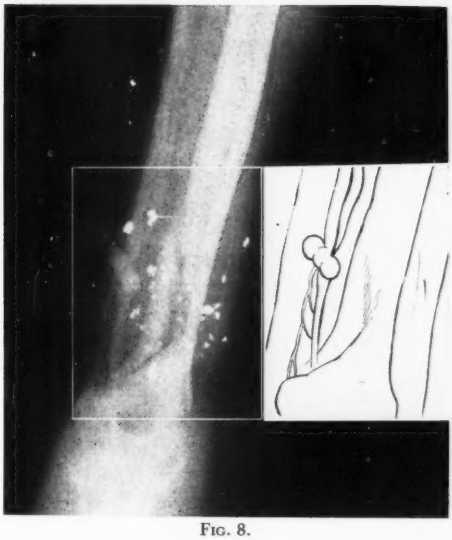

FIG. 8.

in 4 cases with end-to-end anastomoses of the brachial artery. The anastomoses were patent and their locations were imperceptible (Figs. 3 and 4). Five patients were found with symptoms referable to a previous ar-

TABLE I.—SUBCLAVIAN ARTERIOGRAMS OF THE ARM IN 19 CASES

Patient Age Sex	*Indication*	*Method*	*Complications*	*Arteriographic findings*	*Conclusions*
GROUP A—VISUALIZATION OF ARTERIAL ANASTOMOSES IN THE EARLY POSTOPERATIVE PERIOD					
1. A.S. 44 M	Anastomosis of brachial artery after stab wound	Local, percutaneous, 40 c.c. 30 per cent miokon in 9 seconds. One film exposed at 8 seconds	None	Graft is barely perceptible (Fig. 3)	Satisfactory postoperative result
2. J.T.* 39 M	Homograft for multiple birdshot wounds of brachial artery	Same as Case 1, except 30 c.c. 30 per cent miokon used	None	Graft is barely perceptible (Fig. 4)	Satisfactory postoperative result
3. T.W.B. 22 M	Anastomosis of brachial artery after resection of A-V fistula	Same as Case 1, except that multiple films were exposed at ½ second intervals	None	Anastomosis not perceptible	Satisfactory postoperative result
4. J.M.S. 35 M	Anastomosis of brachial artery after resection of A-V fistula	Same as Case 2	None	Anastomosis not pertible	Satisfactory postoperative result
GROUP B—ARTERIAL INSUFFICIENCY DUE TO OLD INJURIES					
5. J.R. 48 M	Brachial artery anastomosis 4 months ago	First attempt unsuccessful due to extravasation. Successfully performed with i.v. pentothal anesthesia during second trial	Extravasation on first attempt caused no difficulty. Slight extravasation at second attempt	Stricture of the anastomosis with poststenotic dilatation (Fig. 5)	Wide resection of stricture was performed and saphenous vein graft inserted
6. N.C. 22 M	Axillary artery anastomosis 1 year previously	Same as Case 2	None	Short area of occlusion with abundant collateral (Fig. 6)	Dorsal sympathectomy was performed for causalgia. Restoration of arterial continuity may be necessary later
7. M.H. 45 F	Injured arm 7 months ago	Same as Case 2	Extravasation of miokon. Slight and temporary cyanosis of fingers required no treatment	Long occlusion of brachial artery. No refilling of distal brachial artery (Fig. 7)	Cervical sympathectomy. Restoration of arterial continuity would require endarterectomy of distal brachial artery
8. T.W.B. 22 M	Bullet wound and supracondylar fracture. Thrill noted 8 weeks after injury	Same as Case 2	None	Brachial A-V fistula (Fig. 8)	Resected with end-to-end anastomosis
GROUP C—ACUTE ARTERIAL INJURIES					
9. J.McD. 35 M	Bullet wound and supracondylar fracture 8 hours before admission. Suspected small A-V fistula	Same as Case 2	None	Brachial A-V fistula	Resected with end-to-end anastomosis
10. H.P. 29 M	Bullet wound with no signs or symptoms of arterial insufficiency. Vague history of spurting blood momentarily	Same as Case 2	None	Filling defect of brachial artery without leak or obstruction (Fig. 11)	Tangential laceration was resected with end-to-end anastomosis
11. E.L. 31 M	Stab wound of axilla. Poor brachial pulse	Same as Case 2	None	Poor brachial pulse is probably due to congenital anomaly with high bifurcation of brachial artery	No exploration indicated
12. C.B. 39 M	Bullet wound of axilla	Same as Case 1	Cyanosis of fingers with venous distention of forearm and hand for 15 minutes. No treatment	No injury	No exploration indicated

TABLE I.—SUBCLAVIAN ARTERIOGRAMS OF THE ARM IN 19 CASES (Continued)

Patient Age Sex	*Indication*	*Method*	*Complications*	*Arteriographic findings*	*Conclusions*
		GROUP C—ACUTE ARTERIAL INJURIES (CONTINUED)			
13. C.D. 49 M	Bullet wound of arm	Same as Case 2	None	No injury	No exploration indicated
14. G.J. 26 M	Bullet wound of forearm	Same as Case 2	None	No injury	No exploration indicated
		GROUP D—CHRONIC OCCLUSIVE ARTERIAL DISEASES OF THE ARM			
15. J.G. 44 M	Marked edema, vesicles, and progressive wet gangrene of arm	Same as Case 2. Percutaneous puncture difficulty	None	Brachial and proximal radial and ulnar arteries visualized in the preamputation arteriogram	Progressive gangrene was apparently due to venous and lymphatic obstruction by subpectoral tumor which required palliative disarticulation of arm. Arteriograms of amputated arm (Fig. 10) showed fresh distal thrombosis. Occlusion of the ulnar artery but no arteriographic evidence of arteriosclerosis such as intimal thickening and calcification
16. R.J. 47 M	Absent ulnar pulse, 10 year history TAO of feet, and now incipient gangrene of toe	Same as Case 2 except multiple films exposed at ½ second intervals	Extravasation at first attempt. Repeated successfully 4 days later	Palmar arch filled via moderately narrow radial and interosseous arteries. Ulnar artery not filled. No intimal disease or localized blocks	
17. E.L.H. M	Recurrent symptoms absent left radial and right ulnar pulse. Quadripedal sympathectomy for arterial insufficiency 5 years ago	Same as Case 2, except multiple films exposed at 1 second intervals	Pain, relieved by stellate ganglion block after arteriogram	Block proximal radial artery and narrow tortuous recanalized distal radial artery	
18. L.R. 35 M	Arterial insufficiency of hands. No pulses at wrist. Had excision right cervical rib and bilateral cervical sympathectomies 5 years ago	Same as Case 2, except multiple films exposed at 1 second intervals	None	Palmar arch filled via enlarged interosseous artery, nonfilling of radial and ulnar arteries	
19. E.L.S. 36 M	Arterial insufficiency and vasospasm mainly of left hand	Percutaneous puncture unsuccessful. Cutdown arteriogram performed under local anesthesia; 25 c.c. 50 per cent miokon injected in 10 seconds; 6 films at 1 second each	None	Palmar arch filled via the interosseous artery. Radial and ulnar arteries not visualized	

*Patient of Drs. C. J. Gaffney and Willard B. Walker (1).

terial injury and the arteriogram was helpful in planning their treatment (Figs. 5 to 8). Because we visualized the palmar arch and proximal digital arteries in many of these cases and because no spasm or other complications occurred, we performed the examination in 5 cases of Buerger's or other occlusive arterial disease involving the hands (Fig. 9). Occlusions of the radial and ulnar arteries have been noted frequently, and the collateral circulation and palmar arch are well demonstrated. Narrow and tapered arteries are seen in Buerger's disease but no intimal plaques are present. The appearance has been quite different from that seen in arteriosclerosis.

In 1 case gangrene of the arm had resulted from the venous and lymphatic obstruction caused by a malignant subpectoral tumor. Arteriograms before amputation demonstrated no abnormality of the axillary, brachial, or proximal radial and

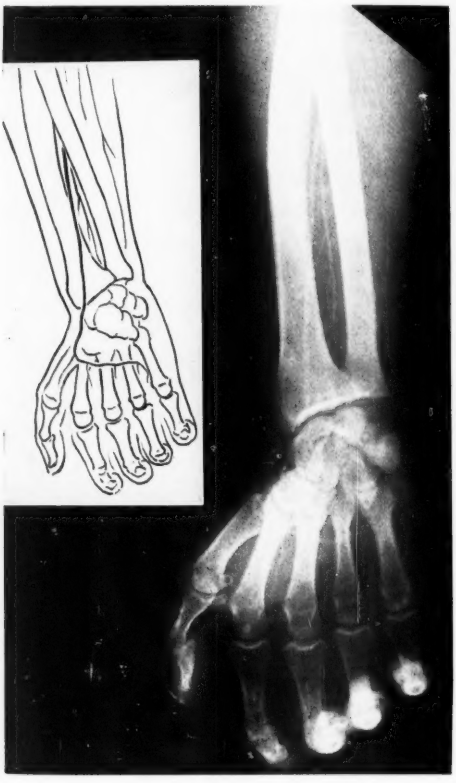

FIG. 9.

FIG. 9. Thromboangiitis obliterans with occlusion of the ulnar artery. The palmar arch and digital vessels fill via the normal radial artery.

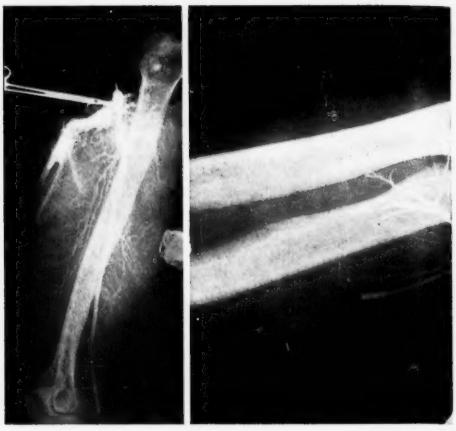

FIG. 10.

FIG. 11.

FIG. 10. Roentgenogram reveals recent thrombosis of all arteries of the forearm.

FIG. 11. Tangential laceration of brachial artery.

ulnar arteries. This observation was confirmed at fasciotomy and subsequently at a palliative disarticulation of the arm. Dissection of the specimen and the postamputation arteriogram showed recent thrombosis of all arteries in the distal forearm (Fig. 10). This condition had developed since the previous arteriogram.

In another case of gangrene of the forearm, blood could not be aspirated from the subclavian artery which was then exposed through a supraclavicular incision and found to be thrombosed.

The diagnosis of arterial injuries is usually easy without arteriograms, and our policy is to explore the vessels in all cases of reasonable doubt. Occasionally, however, arteriograms have been very helpful. For example (Fig. 11), a young man with a gunshot wound above the elbow had normal pulses and no evidence of arterial insufficiency. Blood was alleged to have spurted out of the wound momentarily after the injury. The arteriogram showed a tangential laceration of the brachial artery which was resected with end-to-end anastomosis.

DISCUSSION

The cases illustrate the value of the arteriographic examination of the arms. The

method reported will render a map of the palmar arch and the larger arteries of the arm and the forearm. These findings are useful in the evaluation and differential diagnosis of occlusive or vasospastic diseases before and after operation. To visualize the smallest arteries in the fingers larger volumes or more concentrated dye must be used. Lynn and associates reported results with 50 per cent iodopyracet (diodrast) injected into the brachial artery, but general anesthesia was necessary.

The simplicity and convenience of the method have been gratifying, and although the safety of it will be completely established only after further trial, there have been no complications of note. The success and safety of the method are dependent upon the application of the following principles: (1) the selection of the appropriate position, correct dose of the dye, rates of injection, and timing of the films to fit the particular case; and (2) use of the smallest volume of the most dilute dye that will permit adequate roentgenologic visualization.

Others have advocated surgical exposure of the subclavian or brachial artery. This method has been necessary only once in our series and should probably be avoided because of greater likelihood of spasm. Proximal occlusion of the artery to slow the flow of the injected medium is unnecessary and may lead to spasm also.

The new radio-opaque medium, 30 per cent sodium diprotrizoate has several advantages. Experimental studies by Thomas and associates demonstrate no arterial spasm and these are confirmed by our experience with more than 200 other arteriograms. This property seems important because of the greater frequency and severity of spasm of the arteries of the arm, particularly in vasospastic diseases. An occasional extravasation causes less pain, swelling, and inflammation than other media, and because of the proximity of the brachial plexus this fact seems important. The occasional extravasation has not made subsequent operation more difficult.

CONCLUSIONS

1. The technique of arteriography of the arm by percutaneous injection of the subclavian artery is described. A new radio-opaque material, 30 per cent sodium diprotrizoate has several advantages.

2. This material has been used in 19 cases with no complications, morbidity, or significant vasospasm.

3. The usefulness of the procedure in following brachial and axillary artery injuries postoperatively is demonstrated by a series of cases.

4. Demonstration of the arteries of the hand in vasospastic and obliterative arterial diseases is also possible with minor modifications of the basic technique.

5. As in all arteriograms, careful history and physical examination are necessary to select the appropriate position of the extremity, volume and rate of injection of the medium, and timing of the films.

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MALIGNANT LYMPHOMA OF THE THYROID

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MALIGNANT LYMPHOMA of the thyroid is an infrequent primary lesion. No more than 100 cases have been recorded in the available literature and fewer than 60 of these in the North American literature. Table I gives a compilation of most of the published cases within the last 30 years.

In this article we purport to present an additional 4 cases of malignant lymphoma of thyroid origin, to describe the clinical manifestations and pathologic features, and to ascertain if there is any relationship between malignant lymphoma of the thyroid gland and Hashimoto's disease.

CLINICAL MATERIAL

The material for this study was obtained from 215 cases of malignant neoplasms of the thyroid removed surgically and examined microscopically at The Hertzler Clinic in the 15 year period between 1940 and 1955. Four of these cases proved to be sarcoma originating in the thyroid gland, an incidence of 1.8 per cent. The fifth case presented all the clinical features and followed a typical clinical course of thyroid lymphoma but proved to be a nodular goiter with leukemic infiltration of the thyroid. The enlargement of the thyroid which was the dominant symptom was due to nodular hyperplasia and not to leukemic infiltration. (The pathologic report is included with the case history.)

As shown in Table II the sex incidence of the disease was predominantly female, the sex ratio being 4 females to 1 male. The average age at the time of surgery was 60 years, the youngest patient being 32 and the oldest 73 years of age. The duration of symptoms in all but 1 case was markedly short, varying from 1 week to 3 months; this was particularly true of the enlargement of the neck.

Four of the 5 patients were operated on, with lobectomy performed in 1 case and thyroidectomy done in the remainder. Our second case did not come to surgery but the specimen was obtained by postmortem examination and our diagnosis was confirmed by Graham (personal communication with Hertzler).

In all except 1 of the cases here presented roentgen therapy was given postoperatively. All except the 2 most recent patients died within a 5 month period following both x-ray therapy and surgery. The last 2 patients received roentgen therapy following surgery, with dramatic relief and are at present clinically well.

CLINICAL FEATURES

The signs and symptoms of this disease, both in this clinic and in the recorded literature, have been constant enough to present a syndrome. The patients were predominantly elderly females (average age 60 years), who developed rapid enlargement of the neck with or without pre-existing goiter, accompanied by a tight feeling in the neck with dyspnea, dysphagia, weakness, weight loss, and often hoarseness. Following thyroidectomy and x-ray therapy, the patients experienced marked relief of symptoms and became clinically well for a brief period but then followed a rapidly fatal course within 4 to 6 months.

CASE REPORTS

CASE 1. Female aged 73 years. The admitting complaints were: hoarseness for 3 to 4 weeks, enlargement of the neck for 3 weeks, and dyspnea for 2 days. Phys-

From The Hertzler Clinic and The Hertzler Research Foundation, Halstead, Kansas.

TABLE I.—COMPILATION OF CASES FROM THE LITERATURE

Author	*Date published*	*No. of cases*	*Average age at onset, years*	*Five year survival*
Portmann	1941	12	—	4
Brewer and Orr	1953	10	62.6	4
Dinsmore, Dempsey, and Hazard	1949	8	57.5	0
Lindsay and Dailey	1955	8	60	2
Rice	1932	5	65.6	2
Watson and Pool	1940	5	—	0
Kellett and Sutherland	1949	5	65.4	2
Means	1948	3	57.5	—
Scott	1952	2	62	0
Dick and Kellett	1951–1952	2	61	0
Dean	1949	2	57.5	0
Welti and Huguenin	1939	2	—	—
Roualle	1950	2	68.5	0
Craig and Shepard	1941	1	41	0
Canney	1951–1952	1	74	1
Ambo	1937	1	70	—
Ade	1941	1	54	—
Vaux	1937	1	27	—
Haagensen	1931	1	40	—
Pemberton	1939	4	—	0
Totals		76	60.3	15

TABLE II.—CASE SUMMARIES

Patient Case No. Sex Age, yrs.	*Symptoms*	*Duration*	*Preoperative diagnosis*	*Operation*	*X-ray treatment*	*Follow-up*	*Final diagnosis*
P.L. 1 F 73	Rapid enlargement of neck with dyspnea, dysphagia, weakness, hoarseness	3 wks.	Cancer of thyroid	Rt. lobectomy 11-6-52	2304 r	Died 4-1-52	Lymphoblastoma of thyroid
M.P. 2 F 32	Enlargement of neck, with weakness and weight loss	9 mos.	Cancer of thyroid	No surgery. Autopsy, 3-28-37	0	Died 3-28-37	Lymphoblastoma of thyroid
R.R. 3 F 67	Enlargement of neck, with weakness and weight loss	Few wks.	Nodular colloid goiter	Bilat. subtotal thyroidectomy 1-20-45	1170r	Died 2-25-51	Leukemic infiltration of thyroid; lymphocytic lymphoma
C.H. 4 F 68	Rapid enlargement of neck, with dysphagia, dyspnea, weakness, hoarseness	2–3 wks.	Cancer of thyroid	Thyroidectomy 2-27-57	1500r	Living and well 9 mos.	Lymphosarcoma of thyroid
R.H. 5 M 63	Enlargement of rt. side of neck	3 mos.	Hashimoto's disease	Thyroidectomy 2-21-57	1500r	Living and well 3 mos.	Lymphoblastoma of thyroid

ical examination revealed a bilateral, firm, mobile, thyroid enlargement with a large hard mass in the right side of the neck and an area of dullness to percussion to the right of the sternum below the clavicle. On indirect laryngoscopy, an early lag of the right vocal cord was noted. At surgery, consisting of right lobectomy, the tumor was found to be densely adherent to and invading the carotid vessels above and below the clavicle. The patient received 2,340 roentgens of postoperative radiation. The postoperative course was that of initial improvement followed by a rapid deterioration and death within 5 months.

Grossly, this specimen represented a markedly enlarged right lobe of the thyroid which weighed 52 grams and measured 10 by 8 by 4 centimeters. On the posterior surface was a tracheal groove and on the anterior surface a flat piece of muscle tissue was attached. The lower pole presented tumor tissue protruding through the torn capsule. There were several small nodules of hard consistency about 1 centimeter in diameter on the upper pole, and on the posterior surface there was a nodule measuring 1.8 by 2 centimeters. No definite circumscribed tumor was found on cross section. A mass 6 by 5 centimeters in size replaced most of the tissue. Only in the upper pole could a small area of amber thyroid tissue be recognized. The cut surface of the tumor showed a hemorrhagic center 4 centimeters in diameter. The surrounding tumor tissue was grayish-white and opaque.

On microscopic examination sections from different portions of the tumor revealed a diffuse proliferation of tumor cells, small in size. The nuclei of these

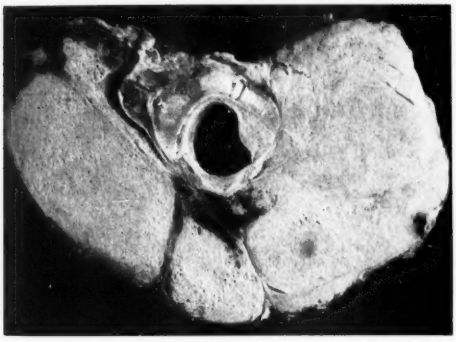

FIG. 1. Case 2. Cross section of lymphoblastoma of the thyroid (autopsy specimen).

cells were round or slightly oval, and no distinct nucleolus was recognized. The cytoplasm in most cells was very indistinct and scanty. In the central portions of the section only occasional small follicles or colloid remnants were recognized. In the upper pole, the tumor invaded tissue between follicles as well as the lumens of the follicles. There was some variation in the size of the nuclei of the tumor cells and some mitotic figures were noted. The nodules on the surface of the right lobe were composed of thyroid tissue, partly invaded by strands of the tumor cells. The reticulum stain revealed a few reticulum fibers which had the tendency to surround groups and strands of cells but did not surround individual tumor cells. The diagnosis was lymphoblastoma of the thyroid.

CASE 2. Female aged 32 years. The admitting complaints were weight loss of 50 pounds in a few months, dyspnea for 3 months, rapid enlargement of the neck for 9 months, and weakness and anorexia for 9 months. On physical examination the thyroid was found to be diffusely enlarged and extremely hard with a large hard nodule in the isthmus. There was no record of

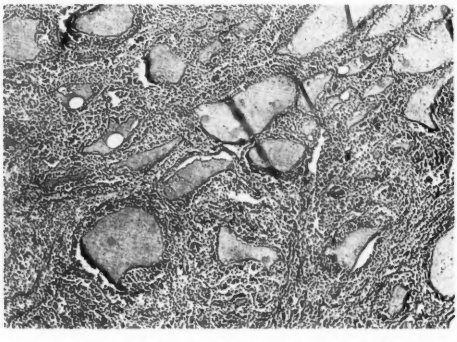

FIG. 2. Case 2. Microscopic section of lymphoblastoma of the thyroid.

indirect laryngoscopic examination. Chest examination revealed a large superior mediastinal mass displacing the trachea. No surgery was done and no x-ray treatment given. The patient died 26 days after admission and an autopsy was obtained.

The autopsy diagnosis was primary lymphosarcoma of the thyroid with direct extension into the mediastinum, with metastases to the liver, kidney, suprarenals, retroperitoneal lymph nodes, pancreas, and both ovaries; multiple ulcers of the stomach with perforation.

On gross examination the upper part of the mediastinum contained a large hard mass continuous with the mass in the neck. When removed along with the mass in the neck, the thyroid could not be identified; the mass seemed to displace or develop out of the thyroid. The trachea was completely surrounded by the tumor, considerably constricting it. The tumor on cut surface presented a smooth white appearance. Spheroidal areas were seen here and there, with larger lobules making up the mass of the tumor (Fig. 1).

On microscopic examination the specimen was found to be composed of large follicles filled with colloid. The normal portions of the thyroid had the appearance of a diffuse colloid goiter. An invasive growth was found on the periphery as well as between the follicles. The tumor cells had the appearance of lymphoblasts with light stained nucleus without distinct nucleolus. The cytoplasm was very scanty and in many cells unstained. No mitotic figures were seen. There was no tendency to form epithelial structures or glandular lumens. The tumor destroyed the follicles and grew into the lumens. The diagnosis was lymphoblastoma of the thyroid (Figs. 1, 2, and 3).

CASE 3. Female aged 67 years. The admitting complaints were of 6 weeks' duration and consisted of recent severe weight loss, a rapidly enlarging lump in the neck, and generalized weakness. On physical examination a large bilateral hard goiter was palpated. Indirect laryngoscopy revealed normal vocal cord excursion. At surgery, consisting of bilateral thyroidectomy, there was no apparent involvement of regional lymph nodes and no apparent direct extension. Roentgen therapy of 2,240 roentgens was given to the anterior and posterior cervical fields. The postoperative course was that of immediate and sustained improvement but the patient succumbed to her disease 6 years later.

On gross examination, the specimen which weighed 57 grams consisted of two lobes, the left measuring 5.5 by 3.5 by 3 centimeters and the right 5.5 by 4 by 2.5 centimeters. A prominent middle process measured 3 by 1 centimeter. The capsule glistened. The cut surface which was amber with whitish streaks showed multiple colloid nodes between 2 millimeters and 2 centimeters in size. Between these nodes was a whitish firm tissue.

At microscopic examination the thyroid was found to consist of indistinct nodes having very large fol-

licles. Most of the epithelium was cuboid but there were many large follicles with cushion-like elevations and columnar epithelium. The colloid was thin and filled out the entire lumen. Many large focal areas of infiltration with lymphocytes were seen. No lymph follicles were noted. The tumor cells resembled mature lymphocytes with dark nucleus and very scanty cytoplasm. The groups of lymphocytes were situated within lobules and in septa. The diagnosis was leukemic infiltration of the thyroid (lymphocytic lymphoma) (Fig. 4).

CASE 4. Female aged 68 years. The admitting complaints were rapid swelling of the neck for 6 weeks (pre-existing goiter), severe dyspnea, and dysphagia of 6 weeks' duration, and weakness with weight loss of 6 to 8 weeks' duration. This patient had been seen 2 years prior to this admission with a hard nodular goiter and had been advised to have immediate surgery. The latest admission was of an emergency nature due to severe dyspnea. Physical examination disclosed that the neck was distended with a hard mass filling most of the left side of the neck; a smaller hard mass was found in the right side. On indirect laryngoscopy an early lag of the right vocal cord was seen. The roentgenogram of the chest revealed that a large superior mediastinal density displaced the trachea markedly to the left. At surgery a decompression operation was done by removing a large mass of tissue from the neck; complete surgical removal of the tumor was impossible. Roentgen therapy of 2,000 roentgens was given to the right and left thyroid areas. The postoperative and posttreatment course was that of complete remission of symptoms and disappearance of the mass in the neck. The patient remains clinically well after 9 months.

Grossly the material consisted of several specimens, one of which had the shape of a thyroid gland, was yellowish-white, firm, and measured 7 by 4.5 by 2 centimeters. The cut surface was yellowish-white and firm. The second specimen was a cylindrical piece of tissue measuring 10 by 5 by 2 centimeters in its maximum dimensions. Cut section of the tumor was made up of yellowish-white tumor tissue. A piece of muscle was identified and seemed to be invaded by the tumor. A small piece of muscle tissue measured 2 by 1.5 by 0.5 centimeter.

On microscopic examination sections from the thyroid revealed areas of typical Hashimoto's disease with small follicles and large oxyphilic cells. Very small adenomas composed of large oxyphilic cells were also seen. Most of the gland showed a diffuse proliferation of large cells with dark nuclei and a distinct nuclear membrane. Many nuclei had nucleoli. The cytoplasm was scanty. Tumor cells were admixed with these lymphocytes and lymphoblasts. There was no tendency to form glandular structures and no transition from the oxyphilic follicles to the tumor cells was noted. In the lymph node most of the tissue consisted of proliferation of reticulum cells which

FIG. 3. Case 2. Metastasis in the kidney from lymphoblastoma of the thyroid.

varied markedly in size. The nuclei of some of these cells were extremely large. There was no evidence of Hodgkin's disease. The association of Hashimoto's disease and the character of the growth favored the diagnosis of lymphosarcoma. The section of the striated muscle showed sheets of reticulum cells invading spaces between the muscle fibrils. The diagnosis was lymphosarcoma of the thyroid with large metastasis in the cervical lymph node, originating in Hashimoto's disease (reticulum cell sarcoma); invasion of cervical muscles (Figs. 5 and 6).

CASE 5. Male aged 60 years. The admitting complaints were a rapidly enlarging lump in the neck for 4 or 5 months and hoarseness and cough for 6 months. On physical examination a bilateral hard nodular goiter was palpated. The vocal cords appeared to be normal on laryngoscopic examination. The roentgenogram of the chest was normal. Surgery consisted of a bilateral subtotal thyroidectomy with no evidence of any malignant extension or invasion. Postoperative roentgen therapy of 2,000 roentgens was given to the anterior and posterior cervical areas.

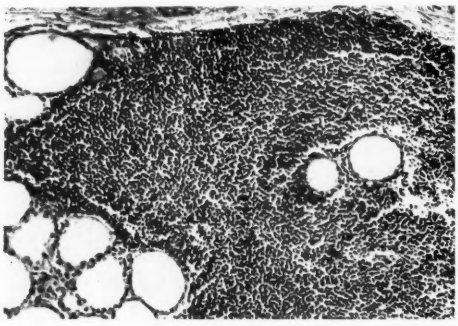

FIG. 4. Case 3. Leukemic infiltration of the thyroid (lymphocytic lymphoma).

After surgery and roentgen therapy the patient experienced complete remission of symptoms and is clinically well 6 months postoperatively.

On gross examination the specimen which weighed 85 grams was found to consist of one large lobe, a large middle lobe, and a small left lobe. The cut surface was light brownish in color and solid with deep lobulation. The right lobe measured 8 by 3 by 3.5 centimeters, the middle lobe measured 5.5 by 3 centimeters and the left lobe measured 2.5 and 2 by 1 centimeter. Sections through the right lobe showed a light grayish-brown cut surface. No nodes were seen. The fibrous tissue apparently was not increased. In the left lobe, small follicles were noted and several areas of dense whitish tissue were seen.

On microscopic examination the right lobe showed very few remnants of thyroid tissue. The follicles were small and some contained groups of monocytes. Very few lymph follicles were seen. Most of the section consisted of diffuse proliferation of round cells which had

FIG. 5. Case 4. Reticulum cell sarcoma of the thyroid with Hashimoto's disease.

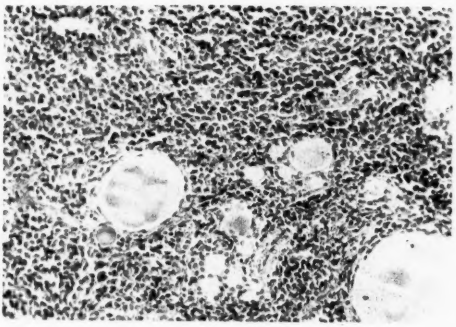

FIG. 6. Case 4. Microscopic section reveals diffuse invasion of the thyroid by reticulum cells.

the appearance of lymphocytes and lymphoblasts although some plasma cells were noted. No giant cells were found. There was no increase of fibrous tissue. Some of the cells were very large and resembled reticulum cells. Sections of the small lobe showed typical Hashimoto's disease with many follicles of various sizes. Most of the smaller follicles consisted of macrophages and contained no colloid. The stroma revealed infiltration with lymphocytes. Some lymph follicles were noted. In this section there was a typical arrangement of the tissue in lobules with fibrous septa. The diagnosis was Hashimoto's disease of the left lobe; lymphoma of the right lobe (lymphoblastic type) (Figs. 7 and 8).

DISCUSSION

The actual occurrence of thyroid sarcoma is difficult to determine because there are no standard criteria of classification and because there is a relative paucity of material. Some observers even question the validity of such a pathologic entity. Other observers like Graham believe that the reported incidence is low and that many cases reported as round cell carcinoma are in reality lymphosarcoma. Anderson states that small cell carcinoma of the thyroid is easily mistaken for lymphosarcoma. Crotti believes that in accordance with more recent observations the round cell carcinoma should be regarded as lymphosarcoma. Pemberton maintains that regardless of some pathologists' skepticism regarding sarcoma of thyroid origin, sarcoma does originate from thyroid tissue and he cites 4 cases.

Certainly the 2 lesions of greatest importance in the differential pathologic diagnosis

are the small round cell carcinoma and the secondary leukemic invasion of the thyroid. Such features as a diffuse single cell infiltration versus a sheet-like cell arrangement, absence or presence of reticulum, and the occurrence of or lack of intimal infiltration aid the pathologist in distinguishing round cell carcinoma and lymphosarcoma, but ultimately it becomes a matter of judgment and experience in pathologic interpretation. The decision as to whether a thyroid is invaded by lymphoma primarily or secondarily is again a matter of judgment based on clinical history and gross pathology as well as the microscopic findings. There are no clear-cut infallible criteria for classification of these tumors.

Distinguishing struma lymphomatosa from lymphosarcoma is no problem for the trained microscopist, but the question of whether or not the lymphosarcoma originates in the struma lymphomatosa is again controversial. The coexistence of lymphosarcoma and struma lymphomatosa is not infrequently mentioned in the literature; there are 2 such cases in this series. This raises the possibility that lymphosarcoma may arise from preexisting struma lymphomatosa. Dick and Kellett discuss such a relationship and state the possibility cannot be excluded but prefer to believe that the lymphosarcoma stems from the lymphoid hyperplasia so often found in the thyroids of elderly females. Lindsay and Dailey found that the thyroid gland of 7 of the 8 patients in their series of lymphosarcoma also displayed Hashimoto's disease. They conclude that a significant relationship exists between the two processes. Dean, Rice, and Wegelin all agree that lymphosarcoma arises in the lymph nodules of the thyroid gland. From our experience and findings we cannot disagree with these viewpoints except to point out that lymph nodules and lymphoid tissue are not normal histologic features of thyroid tissue. When such a finding is present it must be construed as a result of inflammation of the thyroid. In our particular study, 4 cases of lymphoma and 1 case of leukemic invasion have been reported in a 15 year period. In that same period, 202 cases of lymphadenoid goiter were examined microscopically.

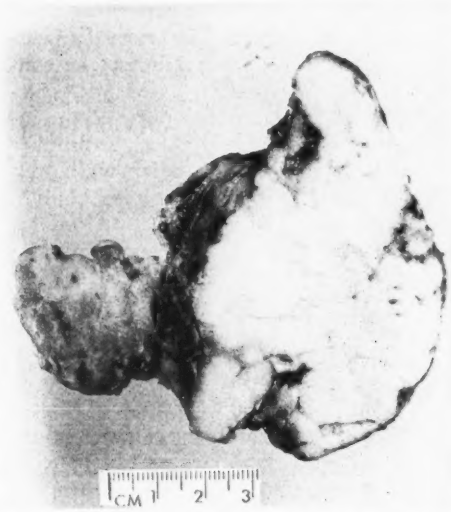

FIG. 7. Case 5. Right lobe—Hashimoto's disease; left lobe—lymphoblastoma of the thyroid.

Brewer and Orr have interjected an interesting concept relative to the survival rate and the histology of the lesion. Four out of their series of 10 patients survived for periods longer than 5 years. This is not the usual outcome as can be seen by referring to Table I. The histology in the fatal cases was identical to the histology of the long

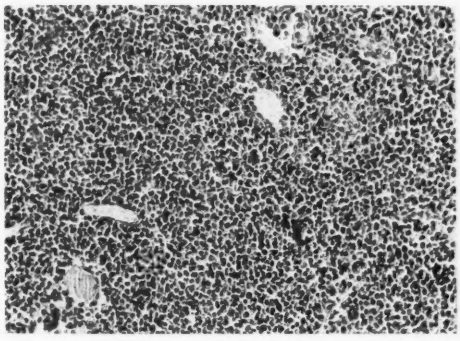

FIG. 8. Case 5. Microscopic section shows only a few follicles still recognizable.

survivals, although the clinical features and clinical course differed. They raise the question as to whether this might not be considered a granulomatous lesion with predilection for the lymphoid tissue of the intestinal wall and thyroid gland. A number of authors have cited like findings with multiple intestinal lesions and a thyroid lesion. Although we have seen this condition twice in our series, the clinical course was rapidly fatal and the clinical and pathologic features remained convincingly consistent with the diagnosis of lymphosarcoma of the thyroid. The findings of Brewer and Orr are interesting but were not implemented or confirmed by this study.

SUMMARY AND CONCLUSIONS

1. Four cases of lymphosarcoma of the thyroid gland are presented with case histories and pathologic descriptions.

2. A compilation of the cases of thyroid lymphoma from the literature of the last 30 years is tabulated.

3. The clinical history of rapid onset of thyroid enlargement, coupled with symptoms of dysphagia, dyspnea, weakness, weight loss, and hoarseness are classical of the disease and are consistent enough to constitute a syndrome.

4. It is believed that primary thyroid lymphoma arises from pre-existing lymphoid tissue present in the gland as a result of inflammation.

5. Attention is drawn to the difficulty of distinguishing histologically thyroid sarcoma from anaplastic carcinoma as well as the primary lesion from malignant invasion.

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HIATUS HERNIA, PEPTIC ESOPHAGITIS, AND PEPTIC ULCER

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INTEREST IN THE TRIAD of hiatus hernia, esophagitis, and peptic ulcer was aroused by a study of 130 patients with peptic esophagitis (3). Thirteen of these patients had this triad and it was strikingly apparent that prolonged efforts at medical management in this particular group of patients was not satisfactory. Stenosis of the esophagus occurred in 6 of these 13 patients.

Benedict and Sweet (2) recognized this triad and reported 6 cases. Three required esophageal resection and 3 prolonged esophageal dilatations. Winkelstein and associates found 5 patients with hiatus hernia among 20 patients with peptic ulcer and esophagitis. In 9 patients esophageal stenosis developed, 4 had massive hematemesis, and 1 had a perforation of the esophagus while on medical treatment.

The peptic ulcer patient with a hiatus hernia seems prone to develop severe reflux peptic esophagitis because of the high acid and peptic contents of the gastric secretions. A study was made of 30 patients with hiatus hernia, esophagitis, and peptic ulcer to discover at what stage in the disease process surgery should be advised and what surgical procedure would be most satisfactory.

CLINICAL MATERIAL

Of 150 patients with peptic esophagitis studied during the past 20 years, 120 patients had an associated hiatus hernia, and 30 patients had hiatus hernia, esophagitis, and duodenal or gastric ulcer. The mean age for the group was 56 years, the oldest patient being 71 years and the youngest 31 years of age. There were 23 males and 7 females.

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The patients' symptoms were those encountered with peptic ulcer and peptic esophagitis. Protracted substernal burning pain and dysphagia marked the onset of esophagitis. The initial symptom in 80 per cent was epigastric pain relieved by foods and antacids. Besides pain, there were acid eructations, gastric distention, nausea, vomiting, anorexia, weight loss, hematemesis, and anemia. The average duration of symptoms of peptic ulcer was 3 years before the onset of substernal burning pain. At least 1 episode of hematemesis occurred in 23 per cent of the patients. In 7 patients esophageal strictures developed. There were 24 duodenal ulcers and 6 gastric ulcers in this series associated with hiatus hernia and peptic esophagitis.

The diagnosis of peptic ulcer was made by gastrointestinal x-ray studies in 95 per cent of the patients, and at the time of operation in 5 per cent. Esophagoscopy was performed in all cases, and the diagnosis of esophagitis made visually or, in the patients with stricture, by biopsy. The hiatus hernia was demonstrated by roentgenography in all but 1 of the patients, and in this patient the hernia was found to be present at the time of operative resection of an esophageal stricture.

MEDICAL TREATMENT

All patients received a prolonged trial on a strict medical regimen. This consisted of an ulcer diet, patient rest, and suppression of gastric motor and secretory activity by the use of antispasmodics, anticholinergics, and antacid drugs. If the symptoms of esophagitis were predominant, patients were placed in reverse Trendelenburg position by elevating the heads of their beds on

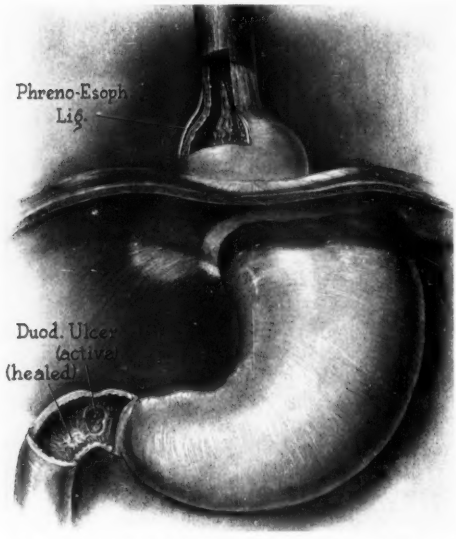

FIG. 1. Cardia of the stomach herniated through the esophageal hiatus. Phrenoesophageal ligament attenuated. Healed and active duodenal ulcer delays gastric emptying and continued reflux of highly concentrated gastric juice results in peptic esophagitis.

8 inch wooden blocks. This procedure was found to be of significant value in preventing gravity gastric reflux at night. Only 4 of the 30 patients were permanently manageable by this medical regimen.

SURGICAL TREATMENT

Unfortunately early in the series surgical treatment was not requested until severe complications of esophageal stricture, hemorrhage, or duodenal obstruction occurred. As a result in 7 cases esophageal strictures developed, 4 of which required esophageal resection. The 3 remaining strictures responded to prolonged antegrade or retrograde esophageal dilatation.

Five patients had a subtotal gastric resection for duodenal obstruction or hemorrhage. The hiatus hernia in these 5 patients was not repaired. Only 1 of these patients obtained a satisfactory result.

Two patients had a vagotomy with gastroenterostomy and transabdominal hiatus hernia repair. Thirteen patients had a gastric resection with transabdominal hiatus hernia repair with excellent results by the technique to be described.

Technique of repair of hiatus hernia—abdominal approach. An upper midline abdominal incision is made from the left margin of the xiphoid process to the umbilicus. Exposure of the esophageal hiatus is obtained by incising the suspensory ligament of the left lobe of the liver and retracting the left lobe of the liver to the right (Fig. 1). The hernia is reduced by traction on the stomach. In order to preserve the phrenoesophageal ligament the upper esophagocardiac branches of the left gastric artery and vein are divided and the peritoneal reflection at the left esophagocardiac border of the stomach is incised. A Penrose drain is passed about the cardia of the stomach through the two incisions in the peritoneum as it reflects upon the cardia of the stomach. The peritoneum and the gastric reflection of the phrenoesophageal ligament are then dissected free of the cardia but left attached to the esophagus (Fig. 2). The stomach is retracted caudally and to the right, and the fibers of the right diaphragmatic crus forming the esophageal hiatus are cleaned, dissected free, and approximated posterior to the esophagus with interrupted No. 00 silk sutures. The esophageal hiatus is closed until it admits only the esophagus and the tip of the index finger. The phrenoesophageal ligament is then sutured to the under surface of the diaphragm (Fig. 3).

In the presence of duodenal ulcer the ulcer is excised with approximately 60 per cent of the stomach, and a posterior Hofmeister type of gastrojejunostomy is performed. For gastric ulcers associated with hiatus hernia and esophagitis the Billroth I type of anastomosis is preferred.

RESULTS OF TREATMENT

Patients were followed for a minimum of 2 years and a maximum of 10 years postoperatively. Only 4 of the 30 patients responded satisfactorily to a medical regimen alone. Two patients required antegrade

esophageal dilatation with prolonged medical treatment. The latter 2 patients were advised to have a gastric resection and a hiatus repair but refused. They continued to have symptoms of duodenal ulcer and esophagitis.

Five patients had a subtotal gastric resection with poor results. Two required prolonged postoperative antegrade esophageal dilatation and 2 a gastrostomy with retrograde dilatation. In 1 patient a complete obstruction due to continued reflux of gastric juices developed and necessitated esophageal resection with esophagocologastrostomy. Esophageal stricture developed after the gastric resection in each of these cases.

Three patients required esophageal resection because of strictures which were allowed to develop following numerous episodes of acute peptic reflux esophagitis. The danger of stenosis was not recognized and attempts at medical therapy were continued until obstruction occurred. The patients were then referred for esophageal resection.

In considering the results obtained in these first 15 patients several conclusions were reached. In patients with hiatus hernia, esophagitis, and peptic ulcer stenosing

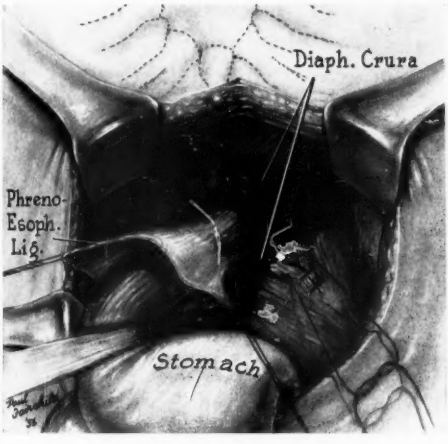

FIG. 2. Phrenoesophageal ligament dissected from cardia of the stomach and its diaphragmatic attachments but left attached to the esophagus. Muscle fibers of the right crus approximated with interrupted No. 00 silk sutures.

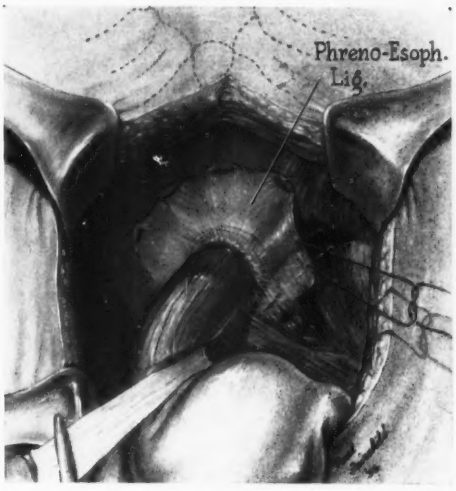

FIG. 3. Phrenoesophageal ligament sutured to the under surface of the diaphragm completing transabdominal repair of hiatus hernia.

esophagitis will develop if the reflux of gastric juice continues. Gastric resection alone may not diminish to a significant degree the production of acid and pepsin, and if the cardiac sphincter is incompetent reflux esophagitis continues. Therefore, all patients have subsequently been treated by repair of the hiatus hernia and gastric resection or vagotomy with gastroenterostomy. Thirteen patients had gastric resection with hiatus hernia repair and 2 vagotomy with gastroenterostomy and repair of hiatus hernia. Results were excellent with both procedures. The results of transabdominal repair of hiatus hernia in this series compare favorably with our results after use of the Allison type of transthoracic repair for uncomplicated hiatus hernia (6). There has been no recurrence of the hiatus hernia in the group of patients in whom transabdominal repair was used.

DISCUSSION

One aim in this article is to emphasize the importance of early surgical treatment in patients with hiatus hernia, peptic esophagitis, and peptic ulcer before the peptic

stenosis of the esophagus occurs because of the inadequacies of medical treatment in this triad. As a result of the study of follow-up on the first 15 patients treated in this group by conservative medical nonoperative measures and in whom surgery was reserved for the complications of the failure of medical treatment a more progressive approach to the treatment has been adopted. Indications for operative repair of the hiatus hernia and gastric resection are: failure of medical measures to control symptoms of esophagitis; the complications of peptic ulcer (hemorrhage, perforation, obstruction, intractable pain) when associated with hiatus hernia and esophagitis or history of esophagitis; and stenosing peptic esophagitis.

Proper surgical therapy should include an anatomic repair of the sliding hiatal hernia and subtotal gastric resection. Technique of repair of a hiatus hernia through the abdomen is patterned after the operative technique of repair through the left thorax as described by Allison and it stresses the preservation of the phrenoesophageal ligament and closure of the enlarged esophageal hiatus by suturing the fibers of the right crus posterior to the esophagus. Several excellent surgical techniques of hiatus hernia repair have been described transthoracically and the importance and technique of preservation of the phrenoesophageal ligament have been stressed. The transabdominal technique of phrenoesophageal ligament preservation and its use in repair have not been adequately described. By careful dissection of the peritoneal reflection on the cardia of the stomach, the phrenoesophageal ligamentous attachments to the esophagus can be preserved and a true anatomic repair of the hiatus hernia be performed transabdominally.

There are certain advantages to the transabdominal approach in the repair of hiatus hernia. As pointed out by Harrington the hernia can be repaired with less risk of injury to the aorta, spleen, and pancreas. Perhaps the most important advantage is complete abdominal exploration for associated disease. Although the presence of other intra-abdominal pathologic conditions can usually be determined preoperatively, in some instances laboratory examination may not reveal their presence. In all patients who have gastric or duodenal ulcers—active or inactive—associated with hiatus hernia and esophagitis the hiatus hernia should be repaired transabdominally.

Results of gastric resection alone without repair of hiatus hernia in this series were not rewarding. This observation is contrary to the results of Wangensteen (5, 7) who reports good results with gastric resection for peptic esophagitis with postoperative esophageal dilatation but agrees with the results reported by others. Another objection to gastric resection without hiatus hernia repair in this triad is that when esophageal resection becomes necessary after subtotal resection of the stomach, the colon or small bowel must be used to re-establish intestinal continuity. A major operative procedure such as this can be avoided if repair of the hiatus hernia is done at the original operation.

SUMMARY

1. Of 150 patients with peptic esophagitis 30 were found to have concomitant hiatus hernia and peptic ulcer of the duodenum or stomach.

2. Medical management of patients with this triad was satisfactory in only 4 of 30 cases.

3. Results of subtotal gastric resection without repair of hiatus hernia were not rewarding in 5 cases.

4. In 7 patients peptic esophageal stenosis developed requiring resection in 4 because of unsuccessful and prolonged attempts at medical management.

5. Subtotal gastric resection with transabdominal anatomic repair of the hiatus hernia is advisable early in the course of disease to prevent esophageal stricture for-

mation. Fifteen patients so treated had excellent postoperative results without recurrence of the hiatus hernia.

6. The anatomic technique of transabdominal repair of esophageal hiatus hernia is described with emphasis on the preservation of the phrenoesophageal ligament and anatomic closure of the esophageal hiatus.

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EFFECTS OF TEMPORARY ISCHEMIA ON RENAL FUNCTION UNDER NORMAL AND HYPOTHERMIC TEMPERATURES WITH AORTIC RENAL GRAFT REPLACEMENT

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THE FEASIBILITY of homograft or prosthetic replacement of the thoracic or abdominal aorta is a well established surgical technique. Hypothermia affords protection by preventing cardiac overloading and preserving spinal cord function incident to acute cross-clamping of the thoracic aorta. Occasionally an abdominal aneurysm or tumor may involve the renal arteries requiring a temporary period of renal ischemia in order to effect resection and graft replacement of the surgical defect.

The experimental survival of animals undergoing temporary renal ischemia under normal temperatures has been reported. There are some specie differences. However, if the critical 2 hour period of temporary ischemia is not exceeded, sufficient renal function persists to permit survival of the experimental animals in most instances. The site of cross-clamping of the renal blood supply is an important factor. In the dog occlusion of the aorta above the renal arteries or of the renal artery alone is well tolerated because of protective distal subfiltration pressures, whereas occlusion of both aorta and renal arteries for the same 2 hour period has resulted in irreversible damage.

Many of the reports of temporary renal ischemia under normal or hypothermic conditions have been experiments in acute cases or in those with short observation periods. The following experiments were performed to study the effect of temporary ischemia on kidney function under normal and hypothermic conditions with long periods of observation.

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SERIES I

A study of the renal function was made on normothermic uninephrectomized dogs following cross-clamping of the remaining renal artery.

Seven female dogs had a preliminary left nephrectomy and episiotomy. One week later renograms were done as a control for renal function. Renographic studies consisted of para-aminohippuric acid (C_{PAH}, renal plasma flow), glomerular filtration rate (C_{cr}), and renal absorptive efficiency ($Tm_{gl.}$). Under endotracheal ether-oxygen anesthesia the remaining renal artery was cross-clamped via a retroperitoneal approach for from ½ to 3 hours. At the end of these time intervals the occluding non-crushing clamps were removed and the laparotomy incision was closed. The surviving dogs were studied periodically by renography for periods up to 123 days.

Results (*Table I*). The critical survival time of cross-clamping the remaining renal artery of a uninephrectomized dog under normothermic conditions was 2 hours. The 3 dogs clamped for 2½, 2¾, and 3 hours died within 4 to 6 days after clamping. The 4 surviving animals which underwent renal artery occlusion of from ½ to 2 hours under normal temperatures showed a recovery of renal function but with a residual impairment. The general picture of re-

covery was gradual over the period of observation. Early, except in dog 2, the initial depression 2 to 5 days after clamping was severe, especially in glomerular filtration and renal absorptive efficiency. Renal plasma flow seemed to be the least affected of the observed kidney functions.

TABLE I.—EFFECTS OF CROSS-CLAMPING THE REMAINING RENAL ARTERY OF NORMOTHERMIC UNINEPHRECTOMIZED DOGS

Dog No.	Wgt. in kgm.	Time of occlusion, hrs.	Glomerular filtration rate, c.c./min.*	Renal plasma flow, c.c./min.*	Renal absorptive efficiency, mgm./min.*	Time in days post-clamping
1	10.6	½	10	75	9	5
			28	74	25	45
			59	83	29	76
2	14.6	1	80	41	80	3
			77	41	73	24
			85	40	65	123
3	10.9	1½	11	80	12	2
			30	87	25	33
			67	83	45	95
4	10.8	2	5	29	4	5
			70	69	61	32
			86	85	65	80

*Values expressed in per cent of normal.

SERIES II

A study was made of ischemic renal injury under normal temperatures followed by renal aortic homograft replacement under hypothermia.

Five female dogs had a preliminary left nephrectomy and episiotomy. One week later renograms were done for a baseline of renal function. Under endotracheal ether-oxygen anesthesia, the remaining renal artery was cross-clamped at normal body temperature for from ½ to 2 hours in order to produce a deliberate ischemic renal injury. A period of time of from 90 to 351 days was allowed for renal recovery following temporary normothermic ischemic cross-clamping. These same dogs were then reoperated upon under hypothermia of 27 to 32 degrees C. by cross-clamping the aorta and renal artery. A segment of renal artery and aorta was excised, and the surgical defect replaced with a fresh homograft. The aortic-renal homograft was inserted in the following manner in order to minimize the time interval of interrupted blood flow to the remaining kidney: (a) double cross-clamping of the host aorta proximal to the origin of the renal artery and severance of the aorta between the clamps; (b) anastomosis of the proximal host aorta with the homograft; (c) double cross-clamping and severing of the host renal artery; (d) anastomosis of the distal renal artery with the renal artery branch of the homograft; (e) removal of the host aortic clamp to below the level of the renal branch of the homograft and removal of the distal renal artery clamp to restore renal blood flow; (f) anastomosis of the aortic homograft to the distal aorta, removal of cross-clamps, and restoration of distal aortic systemic blood flow.

The time of total renal ischemia under hypothermia varied from ½ to ¾ hours. This procedure was carried out in order to evaluate a time which would approximate that required under clinical conditions. By using the methods of retrograde anastomosis mentioned, this arbitrary time of ischemia to the kidney could be reduced.

Results (*Table II*). Three of the dogs survived the long term experiments. The 1 death from renal artery thrombosis 3 days after aortic-renal homografting was probably due to the small size of the renal artery anastomosis. The other death 30 days after aortic-renal grafting followed an aortogram. The added insult of the radiographic media to an already twice injured kidney was enough to produce death from renal injury. Experimental animals in this group again showed a period of depression in all phases of renal function which were studied. The observed period of renal recovery following ischemia under normal temperature was up to 351 days. Only a few animals showed a return to normal or above normal values for the phases of renal function studied (dogs 2 and 4).

Renal recovery following cross-clamping and homografting of the surgically created defect under hypothermia seemed to fol-

TABLE II.—EFFECTS OF ISCHEMIC RENAL INJURY UNDER NORMAL TEMPERATURE FOLLOWED BY RENAL-AORTIC HOMOGRAFT REPLACEMENT WITH HYPOTHERMIA

Dog	*Wgt. in kgm.*	*Time of occlusion*	*Glomerular filtration rate c.c./min.**	*Renal plasma flow, c.c./min.**	*Renal absorptive efficiency, mgm./min.**	*Time in days postclamping*	*Fate*
1	11.8	½ hour	53	50	42	7	
		Normal	37	55	37	37	
		temp.	57	58	35	91	
			66	60	23	211	
		½ hour	HYPOTHERMIA 30.5°C.			313	Renal artery
		Aortic	40	38	13	318	thrombosis—
		graft				321	died
2	11.1	¾ hour	72	77	65	1	
		Normal	39	47	27	41	
		temp.	44	35	64	71	
			110	56	137	100	
			110	77	79	280	
		½ hour	HYPOTHERMIA 30°C.			340	
		Aortic	36	35	33	346	
		graft	69	51	65	386	Died after
						416	aortogram
3	15.4	1 hour	38	50	33	21	
		Normal	67	66	74	135	
		temp.	71	69	69	255	
		½ hour	HYPOTHERMIA 32°C.			351	
		Aortic	38	33	29	353	
		graft	78	60	55	390	
			66	67	67	485	
						535	Sacrificed
4	15.2	1½ hour	16	50	33	4	
		Normal	72	85	77	36	
		temp.	76	65	110	154	
		¾ hour	HYPOTHERMIA 29°C.			161	
		Aortic	21	61	14	192	
		graft	80	65	43	236	
						254	Sacrificed
5	15.1	2 hour	10	10	5	5	
		Normal	83	100	66	30	
		temp.	75	102	68	80	
		½ hour	HYPOTHERMIA 27°C.			93	
		Aortic	64	14	24	95	
		graft	75	50	70	130	
			79	60	72	160	
			70	71	70	218	
						220	Sacrificed

*Values expressed in per cent of normal.

low the same pattern as that observed in the normothermic cross-clamped animals.

CASE REPORTS

The results of the preceding animal experiments led to a clinical application in 2 patients.

CASE 1. W. B., a 40 year old white male, complained of right lumbar pain associated with fever and chills. A palpable nontender, nonmovable mass could be felt extending from the umbilicus to the right costal margin. An intravenous pyelogram showed a nonfunctioning kidney on the right. An exploratory laparotomy and biopsy were done on September 13, 1955. The pathologic diagnosis was inconclusive. "Some areas of the tumor showed sarcomatous changes, others carcinomatous changes compatible with renal cell carcinoma; seminoma could not be excluded." On September 20, 1955 under hypothermia at 30 degrees C. a laparotomy was done. A large tumor mass was resected along with the right kidney and ureter, a thrombosed vena cava, the terminal aorta, and iliac bifurcation. The proximal aorta had to be cross-clamped above the remaining left renal artery. The iliac arteries were cross-clamped proximal to the internal hypogastric arteries with noncrushing clamps. A bifurcated braided orlon prosthesis was used for aortic-iliac replacement. The proximal aorta anastomosis was done, the distal prosthesis cross-clamped, and the proximal aortic clamp removed, thus restoring renal blood flow. The left kidney was without blood flow for ½ hour during this procedure. Both distal

iliac arteries were anastomosed to the bifurcated orlon prosthesis. Occluding clamps were then removed to restore aortic iliac blood flow. The prosthesis was covered with the previously elevated flaps of peritoneum. The final pathologic diagnosis was retroperitoneal seminoma. The testes were normal to palpation. Postoperative nonprotein values were 49, 54, and 35 milligrams per cent on the first, third, and seventh days. Specific gravity of the urine during this period ranged from 1.014 to 1.020. A persistent 1 plus daily urinary albumin was also present. Urinary output was 295, 450, 850, 1,110, 1,500, and 1,900 cubic centimeters during the first 6 postoperative days and thereafter, normal. Renal function studies done 5 months postoperatively showed a renal absorptive efficiency of 70 per cent, renal plasma flow of 65 per cent, and glomerular filtration rate of 80 per cent of normal.

Since the final diagnosis was one of seminoma, 5,400 roentgens were given to the right paravertebral and midpelvic areas. Consideration was given to performing orchiectomy. Six months following surgery the patient was admitted for severe upper gastrointestinal hemorrhage. An upper gastrointestinal series showed a hiatal hernia. Bleeding persisted and a thoracoabdominal exploration was done. A gastrostomy was performed revealing a stomach full of bright red blood with many petechial hemorrhagic areas around the cardioesophageal area. No ulcers were present in the duodenum. A total gastrectomy was performed with a Roux esophagojejunostomy. The patient survived the operation only to die 1 week later of repeated upper gastrointestinal tract hemorrhage. Postmortem findings showed erosion of the orlon prosthesis into the third portion of the duodenum at the site of the proximal anastomosis.

The feasibility of a massive resection of tumor-bearing area along with vital vessel segments was demonstrated in this case in spite of the unfortunate fatal complication. The protection afforded by hypothermia to the one remaining kidney during the ½ hour of renal ischemia is shown. The erosion of the rigid orlon prosthesis may be indicative of the material acting as a foreign body. The role that massive irradiation may have played in this complication is indeterminate.

CASE 2. W. S., a 65 year old white male, complained of a symptomatic abdominal aneurysm of 1 year's duration. A previous exploratory laparotomy had been done but the case was pronounced inoperable since the renal arteries were said to be involved in the aneurysm.

The patient was operated on at the University of Kansas Medical Center on February 28, 1956 under hypothermia at 30 degrees C. The origin of the renal arteries was found at this time to arise 1 centimeter above the aneurysm. This amount of proximal aorta would preclude cross-clamping, resection, and grafting the neck of the aneurysm below the renal arteries. A DeBakey noncrushing aortic clamp was so placed as to occlude the proximal aorta and both renal arteries. The iliac arteries were cross-clamped and the aneurysm was excised. The proximal aortic anastomosis was then made to a nylon prosthesis. The distal prothesis was clamped and the proximal aortic-renal clamp removed to restore blood flow to the kidneys. The kidneys were devoid of blood flow for 25 minutes. The distal aortic anastomosis to the prosthetic graft was then performed in a leisurely fashion. All occluding clamps were removed and the aortic blood flow was restored. The postoperative course was uneventful.

The preoperative nonprotein nitrogen was 36 milligrams per cent and 8 days after surgery was 45 milligrams per cent. Specific gravity of the urine was from 1.014 to 1.020. The daily urinary output for 1 week postoperatively was 650, 475, 1,060, 500, 700, 800, and 1,050 cubic centimeters. Renal function studies done 1 week after cross-clamping and prosthetic aortic replacement showed the following values: renal absorptive efficiency 69 per cent, renal plasma flow 49 per cent, and glomerular filtration rate 58 per cent of normal.

The temporary occlusion of both renal arteries and aorta for 25 minutes during resection and prosthetic replacement resulted in an impaired postoperative renal function. The protection of hypothermia with temporary renal ischemia was further tested in this patient who also had nephrosclerotic kidneys with bilateral renal calculi. Two months following resection of the aneurysm this patient died from hemorrhage. A distal iliac vessel ruptured spontaneously. In the interim prior to fatal rupture he led an active life.

DISCUSSION

Unsuccessful attempts to resect aneurysms involving the renal arteries have been reported by Bahnson (1) and by DeBakey and his associates. The time interval of total renal ischemia of 110 minutes and 105 minutes resulted in fatal termination on the fourth and seventh post-

operative days. Semb reported clamping the renal pedicle for 1½ hours for partial resection of the kidney for renal tuberculosis without evidence of renal damage. Smith, however, stated that the renal pedicle should not be clamped for periods longer than 30 minutes.

Ellis and associates and Bahnson(2) have each reported successful cases following total renal ischemia incident to resection and graft replacement of aneurysms involving the renal arteries.

DeBakey and associates have shown the protection offered by distal subfiltration aortic pressure utilizing a shunt and a retrograde serial anastomosis. The time of total renal ischemia was limited in 3 cases to from 15 to 46 minutes with a return to normal function 10 to 14 days later.

The protection afforded by hypothermia is demonstrated both by the present reported animal experiments and the clinical application to 2 patients. The time of total renal ischemia in these clinical cases was of short duration. This is probably a favorable factor contributing to the successful completion of aortic replacement.

The kidney temporarily deprived of blood under normal and hypothermic temperatures, under the conditions of this experiment, is a damaged organ. Long periods of observation following clamping of the renal arteries show a gradual return of function but never a return to normal.

SUMMARY

The effects of temporary ischemia on renal function under normal and hypothermic temperatures with aortic renal graft replacement are presented.

Two patients were initially successfully operated on for tumor and aneurysm which necessitated temporary renal artery occlusion under hypothermia.

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THE NATURE AND TREATMENT OF THE POSTCOMMISSUROTOMY HYPONATREMIC SYNDROME

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FOLLOWING THE INTRODUCTION of surgical corrective procedures for mitral stenosis there evolved two clinical patterns which have been referred to as the "postcommissurotomy syndrome." One syndrome, characterized by chest pain and recrudescence of symptoms, was described by Soloff in 1953. The other clinical manifestation characterized by oliguria, water retention, hyponatremia, and hypochloremia was described by Wilson and associates in 1954 and Goodyer and Glenn in 1955 and will be referred to as the "postcommissurotomy hyponatremic syndrome." These two clinical pictures apparently are not related since they do not correlate in occurrence. The hyponatremic syndrome occurs in the immediate postoperative period while the chest pain syndrome takes place later in the postoperative course.

The postcommissurotomy hyponatremic syndrome, although frequently transient, can become a problem in the postoperative management of seriously ill patients. Goodyer and Glenn thought that the hyponatremia was secondary to hemodilution resulting from water retention and suggested the possibility of an antidiuretic humoral mechanism. Wilson and associates related an increase in the serum potassium level during the postcommissurotomy hyponatremic syndrome and thought that water retention alone would not fully explain the production of the syndrome.

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Leaf and Mamby reported an abnormal response to water-loading in dogs made hyponatremic by dialysis. In normal dogs measurable antidiuretic activity of the plasma disappeared with water-loading and diuresis occurred. In the hyponatremic dogs antidiuretic activity of the plasma was still detected following water-loading and diuresis did not occur in a normal manner even though hemodilution was produced.

In the study of our patients with the postcommissurotomy hyponatremic syndrome it was noted that they had water retention with a concentrated urine of low volume in the face of hemodilution as evidenced by the low serum sodium and decreased plasma osmolarity. The similarity of this condition and that produced by excessive doses of pitressin together with the observations made by Leaf led to the inquiry of the possible role of the antidiuretic hormone in hyponatremic states. Since alcohol reportedly inhibits the release of antidiuretic hormone from the posterior pituitary and was found to produce diuresis in the state of water intoxication (10), the use of alcohol in the treatment of postcommissurotomy hyponatremia was evaluated.

METHOD

Serum and urine electrolyte measurements and plasma and urine osmolarity determinations were obtained in all patients scheduled for mitral commissurotomy. Daily fluid intake and output data were obtained. When the hyponatremic syndrome occurred postoperative urinary electrolyte excretions were determined daily and the patient was given 20 to 50 milliliters of absolute alcohol

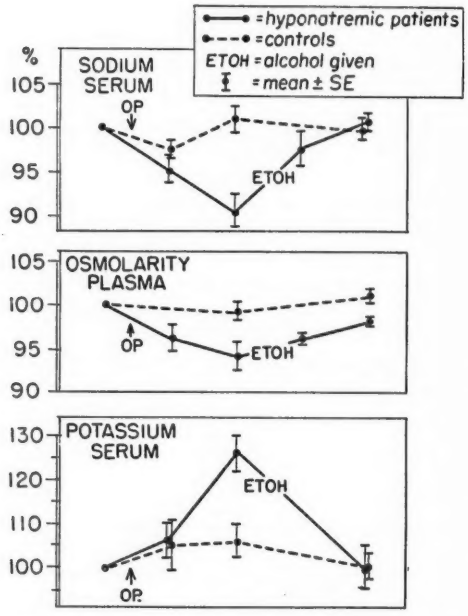

FIG. 1. Illustrating the correlation of the serum sodium and potassium and plasma osmolarity in the control group with the group developing the hyponatremic syndrome; 100 per cent represents the preoperative value.

on the second, third, or fourth postoperative day. The alcohol was given in fruit juice by mouth, or if nausea was present it was given as a 5 per cent intravenous infusion in 5 per cent dextrose in water. The postoperative

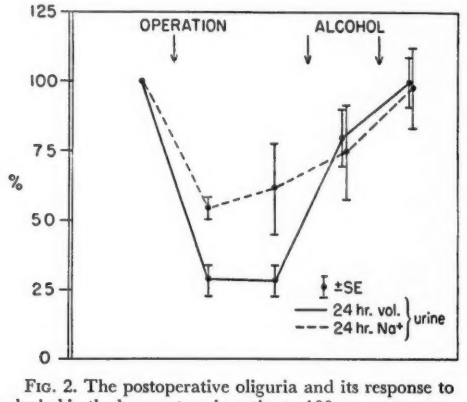

FIG. 2. The postoperative oliguria and its response to alcohol in the hyponatremic patients; 100 per cent represents the preoperative value.

fluid intake was maintained between 1,500 and 2,000 milliliters per day including the alcohol.

Later in the course of the study, daily urine electrolyte excretions were determined during the postoperative period even if the hyponatremic syndrome did not occur in order to obtain comparative urinary excretion data.

Blood samples were analyzed for serum sodium, potassium and chloride concentrations and plasma osmolarity. The 24 hour urine collections were measured for specific gravity, osmolarity, and the content of sodium and potassium. When possible the osmolarity of the urine was measured every 2 to 4 hours.

The patients were maintained on the same low salt diet that they received preoperatively. No supplementary salt was given orally or parenterally.

RESULTS

Twenty-one patients underwent mitral commissurotomy during the period of study. Five developed the postcommissurotomy hyponatremic syndrome. Of the remaining patients complete data were obtained on 8 consecutive postcommissurotomy subjects for control study.

It could not be predicted preoperatively which patient would develop this syndrome after cardiac surgery. In general, however, the occurrence of hyponatremia appeared to correlate with the complexity of the patient's course prior to surgery.

In those patients who developed the syndrome, the serum sodium concentration and the plasma osmolarity decreased appreciably. There was a decrease of 7 to 20 milliequivalents per liter in the serum sodium and a drop of 6 to 20 milliosmols per liter in the plasma osmolarity. The serum potassium rose in 4 of the 5 patients from a preoperative mean of 4.5 milliequivalents per liter to a postoperative mean of 5.1 milliequivalents per liter.

In the control series the serum sodium, serum potassium, and plasma osmolarity re-

mained essentially unchanged following surgery (Fig. 1).

Figure 1 illustrates the comparison of the serum sodium and potassium and plasma osmolarity in the control group with those patients developing the hyponatremic syndrome. The hyponatremia and decrease in plasma osmolarity, an expression of hemodilution, which occurred during the early postoperative period was correctable by alcohol administration. The slight transient decrease in the serum sodium in the controls corresponds with the transient postoperative antidiuresis (Figs. 1 and 4). It is of note that the serum potassium in the group developing the hyponatremic syndrome is increased postoperatively and after the administration of alcohol returns to normal without the urine potassium output returning to preoperative level (Figs. 1 and 4).

The postoperative urinary output of the hyponatremic group decreased to a mean of 28 per cent of their preoperative level and remained at this point until alcohol was administered. In the control patients there was a transient fall to a mean of 47 per cent of the preoperative level with a prompt rise to a mean of 131 per cent on the second and third postoperative days. There was a comparable decrease of the urinary sodium excretion after surgery in both groups. However, the urinary potassium output failed to return to preoperative values in the hyponatremic group even after the diuresis which followed alcohol administration (Fig. 4).

Following the administration of alcohol a diuresis occurred with the 24 hour urine volume being 2 to 6 times the prealcohol 24 hour urine volume. The postoperative oliguria and the response to alcohol administration are graphically demonstrated in Figure 2. The ad libitum preoperative fluid intake was greater than the intake allowed after surgery. Thus, the increase in urine 24 hour volume to 100 per cent of the preoperative value represents a greater urine output per volume fluid intake. The increase in sodium output in the urine was much less than the increase in the urine

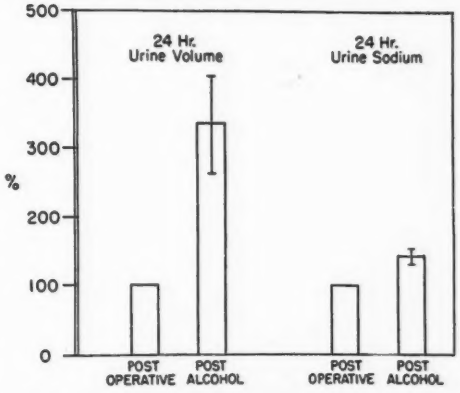

FIG. 3. Comparing the change in urine volume and urinary sodium output following alcohol therapy in patients with the syndrome; 100 per cent represents the mean value during the postoperative oliguric phase.

volume following alcohol administration (Fig. 3). An illustrative case demonstrating the described changes is represented in Figure 5.

With osmolarity determinations performed on the urine at frequent intervals, dilution of the urine as evidenced by a decrease in urine osmolarity to as low as 130 milliosmols per liter during the period of alcohol diuresis occurred. By collecting the urine samples at periodic intervals the decrease in urine concentration during diuresis is more

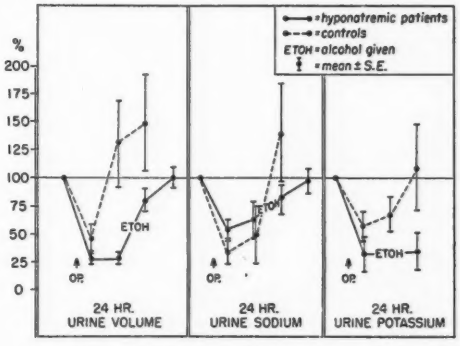

FIG. 4. Comparison of the 24 hour urine volume with the urinary sodium and potassium output in the controls and the hyponatremic group; 100 per cent represents the preoperative value. Note the sustained decrease in the potassium excretion.

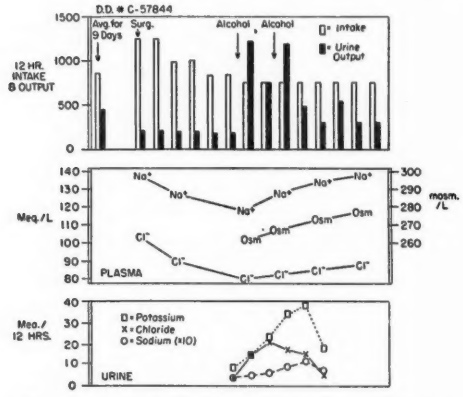

FIG. 5. A case illustrating the occurrence of the hyponatremic syndrome and recovery following alcohol treatment.

readily demonstrated than by studying the 24 hour collection as one sample (Fig. 6).

DISCUSSION

A transient disturbance in the metabolism of water and electrolytes is a common phenomenon during the immediate postoperative period. However, in some cardiac patients these changes are exaggerated and present a clinical problem. It is this group of patients who develop the hyponatremic syndrome with oliguria, water retention, and a concentrated urine in the face of hemodilution. To correct this imbalance the use of alcohol has been effective.

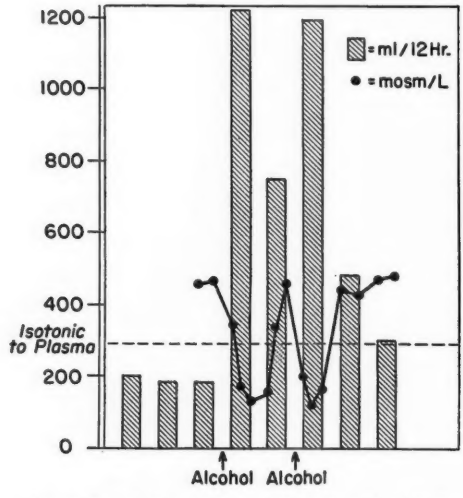

FIG. 6. Correlation of the periods of diuresis with the decrease in urine osmolarity or decrease in urine concentration.

Those patients who developed hyponatremia and hypochloremia did so between the second and fourth postoperative days. The control group showed no tendency to develop this syndrome after the fourth postoperative day. The administration of 20 to 50 milliliter absolute alcohol produced a diuresis within 12 hours in the patients developing the hyponatremic syndrome. The large urine volume with a low sodium content following alcohol administration indicated that the body was retaining sodium and losing water. The diuresis resulted in a return of the serum sodium and chloride and plasma osmolarity to normal.

The serum potassium rose in the hyponatremic patients postoperatively, whereas in the control there was no appreciable change. After the administration of alcohol the serum potassium concentration returned to normal with continued decrease in the urinary potassium output. This phenomenon suggests that the change is due to an extracellular shift, and may be of importance since the 24 hour urine potassium does return to normal in the control group but not in the hyponatremic patients. This interesting relationship is perhaps another effect of the antidiuretic hormone in light of the work of Friedman and associates who demonstrated an extrarenal effect of pitressin in nephrectomized rats.

The exact hemodynamics leading to the stimulation of the antidiuretic hormone in postcommissurotomy patients is not a simple one. Gauer and associates suggested that the oliguria produced by the positive pressure breathing experiments of Drury and associates and the diuresis occurring during negative pressure breathing could be related to stretch receptors in the auricles and great veins within the thoracic cavity. He further postulated that the antidiuretic hormone

could be involved in this phenomenon. Based on these experiments it has been suggested by Sieker that hyponatremia following mitral valvulotomy may be related to reduction of pressure in the left auricle by the valvulotomy. This may explain why the electrolyte imbalance following mitral surgery is more pronounced than that seen after noncardiac surgery. With continued fluid intake there is a retention of water with significant hemodilution and the electrolyte imbalance of hyponatremia, hypochloremia, and an increase in serum potassium. The administration of absolute alcohol inhibits the release of antidiuretic hormone and there occurs a diuresis restoring the serum sodium and chloride and plasma osmolarity to normal. The serum potassium returns to normal possibly as a result of a decreased extrarenal effect of antidiuretic hormone.

One of the most important features that has become apparent during this study is the necessity of fluid restriction following mitral surgery. In patients operated upon after this study there has been a severe limitation of the fluid intake not to excede 1,500 milliliters per 24 hours. In this manner we have been able to avert the occurrence of this hyponatremic syndrome.

That the proposed hypothesis as mentioned before involving the intrathoracic stretch receptors and the antidiuretic hormone is the sole explanation for the cause of the hemodilution and the electrolyte imbalance has not been determined. The possibility that the return of the serum sodium to normal may, in part, be due to a mobilization of this element from another compartment such as bone is under current investigation. However, with the present knowledge, the sequence of events as outlined is tenable.

SUMMARY

The postcommissurotomy hyponatremic syndrome as evidenced by a concentrated urine of low volume, low serum sodium, low serum chloride, increased serum potassium, and electrolyte dilution as evidenced by decreased plasma osmolarity occurred in 5 patients after mitral surgery. Treatment by the administration of absolute alcohol (20 to 50 ml.) resulted in a marked increase in the urinary output with a return of the plasma osmolarity, serum sodium and serum chloride, and serum potassium to normal. Studies of urinary electrolyte excretion during the phase of increased urinary output suggest a true water diuresis with conservation of sodium and potassium. The possible mechanism of the phenomenon is discussed. These studies indicate that alcohol is an effective therapeutic tool in the management of the postcommissurotomy hyponatremic syndrome. The importance of fluid restriction following mitral commissurotomy is stressed.

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EPIDERMOID CARCINOMA OF THE ANAL REGION

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ALTHOUGH EPIDERMOID CARCINOMA of the anal region is not a rare disease it is relatively infrequent. Consequently, detailed analyses of its pathologic behavior and end results of treatment as obtained in recent years are comparatively scarce as opposed to similar studies of adenocarcinoma of the rectum. Keyes, in 1937, published an analyses of 27 cases. In 1954 Grinnell published a comprehensive review of the experience at The Presbyterian Hospital, New York City, of 49 cases. A study of inguinal metastases based on the patients seen at Memorial Center between 1942 and 1952 was published in 1955 (6). The present report is a more inclusive analysis of the patients seen at Memorial Center with this neoplasm. Thus, this is a review of 73 patients having epidermoid carcinoma of the anal region seen by members of the Colon and Rectum Service at Memorial Center during the years 1944 through 1954. This period was selected for study as it not only supplements a report of Binkley of the patients with this neoplasm seen prior to 1944, but it also represented a transition era during which period various forms of therapy were employed and more extended types of surgery were frequently utilized.

MATERIAL

The over-all results obtained in the current series are shown in Table I. Thus, there was an absolute over-all survival of 31 per cent. There were 28 patients who survived 5 years without evidence of recurrent or metastatic disease. Thus, the 5 year survival rate of the determinate group of operative survivors was 47 percent, or 41 per cent when those dying postoperatively were included.

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The results of the various types of therapy are shown in Table II. These figures include the determinate cases only. With the exception of those who had only a preoperative cycle of roentgen ray therapy, those included in the combined therapy group represent failures by one method employed and those in whom attempts were made to control the recurrence by other methods. The breakdown of the combined therapy is shown in Table III.

In reviewing the type of surgery employed, the results are shown in Table IV. It should be emphasized that this represents the initial therapy for the primary lesion. Thus, some of those treated initially by local excision had preoperative or postoperative radiation therapy or groin dissection, either at the time of initial treatment or later in the follow-up period, or in some cases subsequent abdominoperineal resection of the rectum for recurrent disease. Those treated by abdominoperineal resection of the rectum may have had roentgen ray therapy, pelvic node dissection, or groin dissection.

In the group of 18 determinate patients who were treated initially by local excision there were 7 failures. Of this group of 7, 3 had no local recurrence but died of metastatic disease; 1 had local recurrence controlled by abdominoperineal resection of the rectum but subsequently died of metastases; 3 had uncontrolled local recurrences, 2 of which involved bladder and prostate, while 1 was unsuccessfully treated by roentgen ray therapy. In the group of 11 who were successfully treated, 6 had no local recurrence; 3 had local recurrences successfully treated by re-excision locally; and 2 had local recurrences controlled by abdominoperineal resection. Thus, the deaths of 4 of this group of 18, 22 per cent, might be attributed to inadequate initial surgery.

Obviously the results obtained by local excision cannot be compared with those obtained by abdominoperineal resection of the rectum, as the latter patients had lesions which were from the beginning larger lesions not considered suitable for local excision. Nevertheless, it is seen that 6 patients initially treated by abdominoperineal resection of the rectum had local recurrences, in spite of the more extensive local removal.

TABLE I.—OVER-ALL RESULTS OF SERIES

		No. of patients
Total patients seen, 1944–1954		74
Indeterminate patients		15
Treated elsewhere; evaluation only	4	
Postoperative deaths	3	
Lost track of, died of other causes without evidence of disease	8	
Failures		34
Less than 5 years	31	
Over 5 years	3	
Successes		25
Over-all survival rate, 25/74, per cent		31
Five year survival-determinate, 28/59, per cent		47

SITES OF METASTASES

It has been indicated that epidermoid carcinoma of this area rarely if ever metastasizes to the liver. However, in this series of 59 determinate cases, in 7 or 12 per cent, clinically obvious liver metastases were observed.

Obviously we cannot state how many patients in the entire series had metastases along the superior hemorrhoidal lymphatic pathways which lie in the mesorectum. However, of 31 patients treated by abdominoperineal resection of the rectum, 7, or 23 per cent, did have metastases along this route. This is in keeping with Grinnell's findings. Of 5 in the determinate group who had metastases to the mesenteric nodes, only 1 survived 5 years free of disease.

By pelvic nodes we refer to those nodes within the pelvis not removed by the ordinary type of Miles resection, i.e., the sacral promontory, the common, external and internal iliacs, and obturator nodes. Again, we cannot state the over-all incidence of metastases to these nodes. However, of 19 patients studied, the specimens being obtained either by radical groin dissection or pelvic lymph node dissection in conjuntion with abdominoperineal resection, 9 or 47 per cent, did have metastases to these nodes. In 4 of the 9 patients, the metastases were removed by pelvic lymph node dissection at the time of abdominoperineal resection of the rectum. None of these survived 5 years. In the remaining 5 patients, the metastases were removed by radical groin dissection performed at a later date when superficial groin metastases became evident. Three of these patients survived 5 years free of evidence of recurrence.

Of the 58 determinate cases, superficial groin metastases were clinically evident in 27, or 46 per cent. All but 3 were histologically confirmed. Prophylactic groin dissections were not done in this series. It is possible, but unlikely, that metastases that were never clinically recognizable were present. This is one of the highest reported incidences of groin metastases with this neoplasm. Of the 27 patients with groin metastases, the nodes were clinically positive on admission in 15. In spite of accepted therapy none of these patients survived 5 years. In 12 patients no clinically suspicious nodes could be detected on admission but appeared subsequently. Of these 12, 5 were successfully treated, living 5 years without subsequent evidence of recurrence or metastases, a 40 per cent survival rate. Of the 7 who were not successfully treated, 2 had uncontrolled local recurrences, 1 had liver metastases, and in 1, the groin metastases became evident 9

TABLE II.—RESULTS OF TREATMENT

		No. of cases
Palliative; liver metastases at operation		1
X-ray only		13
Failures	11	
Five year survivors without evidence of disease	2	
Five year survival rate, per cent	15	
Surgery only		18
Failures	5	
Five year survivors without evidence of disease	13	
Five year survival rate, per cent	72	
Combined x-ray and surgery		26
Failures	15	
Five year survivors without evidence of disease	11	
Five year survival rate, per cent	47	

TABLE III.—COMBINED RADIATION AND SURGICAL THERAPY

	Total No.	*No. of 5 year survivors*	*Per cent, 5 year survival*
Preoperative x-ray therapy.....	11	3	27
Recurrence after radiation, subsequent surgery.....	8	5	63
Recurrence after surgery, subsequent radiation therapy....	4	1	25
Recurrence after surgery, uncontrolled by subsequent radiation, subsequent surgery.....	4	3	75

years after treatment of the primary lesion.

Two patients have had lung metastases. One patient had spine metastases, and 1 had multiple skin implants.

DISCUSSION

While epidermoid carcinoma of the anal region is generally thought to have a considerably poorer prognosis than adenocarcinoma in the same area, the over-all 5 year survival of determinate patients (including those who died postoperatively) in this series was 40 per cent as opposed to a 34 per cent 5 year survival of determinate patients with adenocarcinoma of the rectum seen at Memorial Center during the years 1947 and 1948. This observation is in accord with Grinnell's conclusion based on the series at Presbyterian Hospital. The results seem comparable also to those reported by Judd and Detar from the Mayo Clinic.

In the past we have generally considered that epidermoid carcinoma in this region defined its outcome rather rapidly; however, of 28 patients in this series who lived 5 years free of recurrence or clinical evidence of metastases, 3, or 10 per cent eventually died of the disease.

Epidermoid carcinoma of the anal region, although not rare is so infrequent that its treatment has not been standardized. Roux-Berger reported a 35 per cent 5 year survival rate obtained by radiation therapy as the sole agent. Sweet reported only one 5 year survivor of 19 treated by radiation methods. Although the present series is weighted heavily by those who had surgical treatment, there were 13 treated by roentgen ray therapy of whom 2 or 15 per cent survived 5 years without evidence of recurrence or metastases.

From the data we have (Table III), we are unable to evaluate properly the role of preoperative or postoperative radiation therapy in combination with surgery. We are not aware of any such study in the literature.

In considering the possible advantages of combined therapy as shown in Table III there was 1 patient whose tumor recurred following surgery who was salvaged solely by subsequent radiation therapy. There were 5 out of 8 who were not controlled by initial radiation therapy who were salvaged by subsequent surgery.

In considering the proper surgery for patients with these lesions various possibilities should be considered. The first is whether it is justified in selected cases to attempt local excision. As we have indicated in Table IV, 4 patients, and 1 of these is equivocal, out of 18, 22 per cent, had local recurrence following excision and eventually died; these failures should probably be considered due to inadequate initial treatment. Three were uncontrolled, the fourth was controlled locally by abdominoperineal resection but liver metastases developed shortly thereafter. There is some indication that some of these patients had lesions which were more extensive than are considered suitable for such a procedure at the present time. Nevertheless, the 22 per cent represents the maximum hazard associated with local excision in selected patients. This therapy is to be compared with routine abdominoperineal resection of the rectum with permanent colostomies for all patients with this neoplasm.

In considering possible factors that might be of value in selective patients for initial local excision we could not demonstrate that the size, the location, or the histologic grade of the primary tumor provided a reliable guide. However, the data available for analysis were rather meager and are not considered conclusive.

In deciding the extent of operation, if other than a local procedure is to be done, the sites of metastases should be a basic consideration. In this group of patients, metastases along the superior hemorrhoidal chain were present in roughly 20 per cent of those studied. This represents a selected group of patients whose primary lesions were so invasive locally, as to warrant abdominoperineal resection. Pelvic lymph node metastases were present in 45 per cent of those studied. This also is a selected group of patients whose primary lesions warranted abdominoperineal resection or who developed superficial groin metastases. Superficial groin metastases were present in 45 per cent of the patients followed. Theoretically, the high incidence of metastases to each of these areas would indicate that ideal operations should include excision of each region.

Theoretic procedures should be evaluated in terms of the results obtained. In this series of those patients who had lymph node metastases at the time of initial treatment of the primary lesion, none with groin or pelvic node metastases was cured. One of 5, 20 per cent, with mesenteric node metastases lived 5 years free of disease.

When abdominoperineal resection of the rectum is performed, the mesenteric lymphatics are removed. Pelvic node dissection can be incorporated in this procedure without added mortality and with a permissible morbidity to the patient. Even though we have failed to salvage any patient in whom pelvic lymph node metastases were removed as part of this procedure, our experience is still too meager to state unequivocally that it will not eventually prove effective in sufficient number to warrant its continuation in patients with this neoplasm.

In considering the desirability of groin dissection at the time of initial treatment in those patients without clinically involved nodes, our experience is summarized as follows: There were 12 patients in whom no clinically positive groin nodes could be detected at time of initial therapy but in whom metastases appeared subsequently. Five were successfully treated by therapeutic groin dissection. Of the 7 who were not cured, 2 had uncontrolled local recurrences; 1 had liver metastases; in 1 the groin metastases appeared 9 years after treatment of the primary lesion, and the patient did not return for 1½ years for treatment of the metastases which had been diagnosed elsewhere as a hernia.

TABLE IV.—SURGICAL RESULTS

	No. of cases
Local excision—initial treatment	18
Failures	7
No local recurrence; metastases	3
Local recurrence	4
Uncontrolled locally	3
Controlled locally by abdominoperineal resection; died of metastases	1
Successes	11
No local recurrence	6
Local recurrence	5
Controlled local excision	3
Controlled by abdominoperineal resection	2
Five year survival rate, per cent	61
Abdominoperineal resection	27
Failures	13
Local recurrence	5
Successes	14
Local recurrence—x-ray	1
Five year survival rate, per cent	52

Thus, if bilateral prophylactic groin dissection had been done routinely, there were possibly 4 patients out of the determinate group of 43 suitable for such treatment who might have been salvaged. However, not 1 of the patients who had groin node metastases at the time of initial treatment was salvaged by groin dissection or other therapy. The not inconsiderable morbidity that accompanies bilateral groin dissection should be weighed in considering such routine "prophylactic" procedures.

It may well be, when the end results are published by the authors advocating routine bilateral prophylactic groin dissection as part of the management of this neoplasm, that these will indicate the value of this procedure but such evidence is not presently available.

Obviously the material presented is subject to various interpretations allowing more than one conclusion as to what constitutes

acceptable treatment for epidermoid carcinoma of the anal region.

The present policy of the Colon and Rectum Service at Memorial Center, which we believe is in keeping with the data that we have accumulated may be outlined briefly. Patients with small perianal lesions are treated by wide local excision of the primary neoplasm. The site of such excision is examined at monthly or bimonthly intervals. The groins are followed carefully and if and when nodes become evident, unilateral radical groin dissection is done. Those patients whose lesions are more extensive, involving the anal musculature or infiltrating into the perianal tissue adjacent to the sphincters are treated by abdominoperineal resection of the rectum with pelvic node dissection. The groins are observed and superficial groin dissection is done on the side when and if indicated.

SUMMARY

1. A series of 74 patients with epidermoid carcinoma seen at Memorial Center between 1944 and 1954 is reviewed.

2. Forty-one per cent of the patients treated for cure, who could be traced, had survived 5 or more years.

3. The 5 year survival rate of those treated by roentgen ray alone was 15 per cent, by surgery alone 72 per cent, and by combined radiation therapy and surgery 42 per cent. The majority of those salvaged by combined therapy represented successful surgery after unsuccessful radiation therapy.

4. In 18 cases in which local excision was used as initial therapy, there were 4 deaths (22 per cent) which might have been avoided had more radical surgery been used initially.

5. The sites of metastases in this series were: the liver in 12 per cent; mesenteric lymph nodes in 23 per cent; pelvic lymph nodes in 47 per cent; superficial inguinal lymph nodes in 46 per cent; lung in 3 per cent; and spine in 2 per cent.

6. The outline of therapy being used at present follows: (a) Small perianal lesions are treated by wide local excisions. The patients are examined at 1 to 2 month intervals. Unilateral radical groin dissection is done when the nodes become involved clinically. If there is local recurrence an abdominoperineal resection with pelvic lymph node dissection is usually carried out. (b) More extensive or infiltrating perianal lesions and lesions involving anal canal and sphincters are treated by abdominoperineal resection of the rectum with pelvic lymph node dissection. The patients are examined at 1 to 2 month intervals with particular attention to the groins. A unilateral superficial groin dissection is done when, and if, the nodes become involved clinically.

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ALLEN O. WHIPPLE, M.D.

Still Life of Mushrooms

EDITORIAL

CAN CERTIFICATION BE SEPARATED FROM GRADUATE EDUCATION IN SURGERY

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THE CERTIFYING BOARDS in the field of surgery now have a position of great influence on the educational, civic, and economic phases of surgery. Not all of this was intended, and responsibility for it is often denied in the preambles of their requirements. They emphasize that they are examining and certifying bodies created to evaluate competence in their respective fields. This is true, but in so doing they have set up requirements for residency training as a prerequisite to their qualifying examinations. At first these rules were stated in broad general terms that were liberal enough to allow freedom of the individual or institution to meet the requirements in a variety of ways. But as the economic and professional consequences of board certification increased, there was strong motivation for residents to seek it at any cost and for hospitals to gain approval for residency training without regard to their capacity in education. This led to tighter rules by the boards, by the American Medical Association, and by the American College of Surgeons. These rules were honestly designed to elevate the standards of competence, but as weaknesses developed more rules were required so that now they have become restrictive. There is an appreciable loss of freedom and an inclination to press everyone into the same mold. Should one ask the members of these regulatory bodies if they believe that everyone is intellectually equal or if the best methods of achieving competence in surgery have been found, the chances are they would deny this, but the rules they make affirm it. Certainly regulation, regimentation, and a stereotyped product is being demanded.

The basic difficulty is that regulatory bodies have invaded the field of graduate surgical education despite the fact that they are not educational institutions. Residency training is not an exercise in manual dexterity, nor is it a trade school, but rather is graduate surgical education and, as such, belongs under the jurisdiction of the medical schools. If, for example, the surgical specialty boards went back to their original purpose of examining and certifying for competence and left to the professors of surgery in our accredited schools the decision of what is required for acceptable graduate surgical education they would not only eliminate many of their present troubles but also would place this phase of the subject in its proper perspective. The chairman of a department of surgery is in the best position to know the complex interrelationships between undergraduate and graduate education. In the university clinic, he fosters, develops, and integrates all the branches of surgery. He cannot confine his interests to only one

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specialty since he is charged with the final responsibility for the teaching and practice of all the specialties of surgery in his institution. In his daily life, he must try to coordinate the conflicting rules of the various specialty boards and of other regulatory bodies with the over-all curriculum. Since the professor of surgery must see all of the perimeters of graduate surgical education, he is in the best position to decide on its needs. Teaching is his business, and residency training is the graduate teaching of surgery.

Is it an idle dream to hope that examination and certification of competence be separated from the educational process that leads up to it? Not if the examination is broad and searching enough to evaluate competence. If boards wished to screen candidates for their fitness to be examined, this could be done on an individual basis. They could even point out to the candidate what prerequisites have, in their experience, given the highest degree of success in passing their examination. But when they specify the way to become competent, they encourage adherence to the letter rather than the spirit of their rules. This has led many candidates to desire only to meet board requirements rather than to acquire proficiency and for many hospitals, without educational facilities, to create half-baked residency programs which do not remotely resemble what the members of these boards had in mind and which Halsted would never recognize as such. Qualification then becomes an exercise in semantics not surgery.

Is it practical to dissociate the examination for competence from the preparation for that examination? A quick answer would be that the Royal College of Surgeons has done this. But more thoughtful consideration would lead to the opposite question; can we afford not to separate the two? For, as the economic rewards of board certification by schools, hospitals, government agencies, courts, and insurance companies increase, then the act of certification develops a profound consequence on professional life. It is literally a union card to practice. This is an expression of the need, in our society, for some yardstick to distinguish the competent from the self-styled specialist. It is not the fault of the boards, but it places a heavy responsibility upon them. Their certification becomes a judgment that has far-reaching consequences. They must constantly seek just and equitable but thorough methods for evaluating competence. This is a big job in itself. If, in addition, they try to specify the details of graduate education they are apt to dissipate their energy in a field that belongs to the medical schools and so neglect their primary responsibility. The conclusion is reached that it is not only practical but mandatory to separate the evaluation of competence from the variety of ways in which it may be achieved.

The boards of the various specialties of surgery have never co-ordinated their programs with one another. They could never get together on such a fundamental issue as the amount of general training in surgery which was desirable before starting specialization. This general training is often erroneously spoken of as "general surgery" but it is not limited to that division of surgical specialization. Rather it is designed to give a comprehensive view of the principles of surgery as a whole. To quote the American Board of Surgery, this consists of "knowledge of the basic principles applied in the treatment of fractures, trauma, head injuries and the more common procedures in plastic, gynecologic, orthopedic, thoracic and urologic surgery." It may, and usually does, include some correlation of the basic sciences and surgical pathology. In the past, this comprehensive experience was considered a necessary part of any well organized residency training program, and in university clinics 2 or 3 years were devoted to it. Since this period allowed the resident to explore and develop his interest in some one of the subdivisions of surgery, it was a means of recruitment for all specialties. It permitted the staff to evaluate the aptitudes of the

resident so that he could be honestly advised on the choice of a career and how to attain it. Finally, it gave a broad, comprehensive foundation, on which to build the knowledge and skills required for a special field. Except in plastic surgery this is no longer possible. Even in general and thoracic surgery, when certification by the American Board of Surgery is obtained under group II by 3 years of residency plus 2 years of preceptorship, such a broad program of general training in surgery is difficult. Those who qualify in this way must have 3 years which is "graded" and entirely "clinical." Credit is not allowed for time spent in research or a preclinical subject. This program eliminates an assignment to surgical pathology despite the fact that an important part of the examination given by this board is in that subject.

The elimination of a broad, general training in surgery has gone further in some of the other surgical specialties. In ophthalmology, otolaryngology, and anesthesiology, only a year's internship (which may be rotating) is required before specialization. In orthopedic, neurologic, and urologic surgery, at least 1 year of general training in surgery is accepted but in none of these is it required. For example, the candidate in neurosurgery can limit his 4 years of residency to that field without knowledge of or time spent in any other area of surgery. (One wonders what Cushing would say to this.) Moreover, the majority of the surgical specialty boards now require 3 years of specialized training. This has been achieved at the expense of a broad general training despite the fact that many eminent specialists, in fact some members of these very boards, were trained by a judicious combination of the two. As the knowledge in any special field increases, it is quite natural to expect that more time is needed to encompass it. But this can be pushed to the point of diminishing returns. If limited specialization in surgery begins after the internship, then recruitment into that specialty may be diminished, premature decisions on a lifetime career be required, and a narrow perspective, with a "keyhole point of view," obtained. These conditions may militate against the full development of a special field. Yet the rules for certification in these fields have never recognized this fact.

At this stage, the prospect of re-evauluation and reorganization of graduate education in the entire field of surgery appears remote. Probably there is one group, and only one, who can do this. If the professors of surgery in the medical schools of this country could agree, and there is a surprising unanimity of opinion among them, on what are the aims of specialization in the fields of surgery and how these objectives can be attained, then by concerted action they could influence graduate surgical education. For example, if they decide that a period of broad general training in surgery was desirable before specialization in one of its branches, they would only have to say that in their university clinics this must be done. If this action was concerted then it would not be long before others followed suit.

But this is only one facet of a much broader responsibility of the medical schools and their departments of surgery. They must assume the task of guidance in graduate education in surgery in order to end attempts at education by edict; to emphasize that the quality of the product, not the means of producing it, is the aim; to affirm that proficiency can be achieved in many ways and that the goal, not the road to it, is important; to deny that all men are intellectually equal and when subjected to a stereotyped process, like so much raw material in a production line, that they will all come out equally bright; but, most important of all, to guard and cherish the freedom for experimentation in graduate surgical education to meet the economic and scientific changes in surgery which is by no means static.

THE SURGEON AT WORK

A SURVEY ON EARLY AMBULATION AFTER SURGERY

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THE REPLIES received to a questionnaire addressed to the surgical departments of leading medical schools and hospitals throughout the United States demonstrate that early ambulation after operation—which was virtually unknown in our hospitals 15 years ago—has found practically universal acceptance, at least in theory. A more detailed analysis of the material representing the experience and opinions of the surgical staffs in 29 University hospitals and 54 private hospitals, however, indicates that, while the idea of early ambulation has been generally accepted, the inconsistencies in its application in practice still reveal incomplete understanding of the principles and rationale of the procedure.

FACTS ELICITED BY THE QUESTIONNAIRE

The time of the first ambulation after various operations, as practiced in the 83 hospitals responding to this questionnaire, is indicated in Table I, which is self-explanatory. In compiling the data, the earliest period of ambulation noted on the questionnaire was used, although this does not signify that all surgeons in the hospital get their patients out of bed at the same time. Some hospitals did not report the time of ambulation after certain procedures; for example, only 53 furnished information on intervertebral disk resection. These and other omissions were not explained.

The surgeons who insist that patients get out of bed immediately on recovery from anesthesia, or on the day of operation, still constitute a small minority. Only 3.5 per cent report immediate ambulation on recovery from the anesthesia; 9.8 per cent on the day of operation; 43.4 per cent on the first day after operation; 14.7 per cent on the second day after operation; 7.8 per cent on the third day, and 4.3 per cent 4 or more days after surgery. In 17.8 per cent, the time of the first ambulation was not mentioned.

Answers from the various institutions indicate, in most instances, considerable discrepancy in the use of ambulation by individual surgeons on the staff. In some hospitals, some surgeons prescribe ambulation immediately on recovery from the anesthetic, while others delay ambulation as late as the fifth or sixth day. Some surgeons require all of their patients to ambulate immediately after recovery from anesthesia or on the day of operation, while others in the same specialty in the same hospital may delay ambulation until the first or second or third postoperative day.

Besides the differences among surgeons on the same hospital staff, the questionnaire also indicates that individual surgeons are inconsistent in their use of early ambulation. Fifty-six replies indicate that ambulation is withheld in some cases, even by those who advocate its use generally. For example, some surgeons exclude ambulation after certain procedures, such as abdominoperineal resection or gastrectomy, until several days after operation. Some believe that ambulation is contraindicated after any extensive procedure, especially when the patient appears very ill. Others admit that they do not require patients to walk, that is, if they object or "do not feel like doing so." In 42 hospitals, "dangling" is used prior to ambulation by at least part of the staff. Answers from 28 hospitals indicated that dangling is not permitted as a preliminary preparation for ambulation. Only 29 insist that early ambulation be carried out vigorously (that is, in cases in which it is routinely used), while 23 stated that they are moderately insistent and

15 admitted that walking after operation is not insisted upon, but is left up to the discretion of the patient. Nine answers indicated that the patient is required to walk only once each day; 39, twice a day; 11, three times daily, and 5 stated that ambulation is prescribed 4 to 8 times daily. Forty replies stated that activity and exercise are limited after discharge from the hospital, while 31 replied that no limitation of activity is advised after dismissal. Two bar heavy lifting only.

Seventy answers specifically stated that early ambulation hastens recovery (5 of these were very emphatic). One answered this question in the negative, and 4 were not sure. Seventy-one reported no ill effects from early ambulation, while 5 mentioned some type of complication related to this procedure. For instance, one surgeon who prescribes the first ambulation from 1 to 3 days after operation cited 1 instance of wound dehiscence on the eighth day. Another who keeps his herniorrhaphy patients in bed until the fifth postoperative day said that early ambulation increases hernia recurrence. This discrepant opinion is striking in view of the fact that early ambulation is more widely and consistently used after hernial repair than after any other operation. Another individual whose patients ambulate on the first day after operation mentioned hemorrhage. Two other individual surgeons, who prescribe the first ambulation on the second and third days after operation, respectively, did not specify what late complications they had seen. Strictly speaking, none of these surgeons who mentioned complications actually uses early ambulation which could be expected to yield the most effective results.

Forty-five hospitals answered that ambulation is believed to prevent postoperative atelectasis and pneumonia, 14 that it probably reduces the incidence. Eleven believe that ambulation does not prevent postoperative pneumonia, and 12 were doubtful or not sure about its effect. As for pulmonary embolism, 39 believe that it is prevented by early ambulation; 14 that it probably reduces the incidence. Seventeen believed that pulmonary embolism is not reduced or prevented by early ambulation, and 12 were doubtful or noncommittal.

TABLE I.—ANALYSIS OF REPLIES TO QUESTIONNAIRE ON EARLY AMBULATION AFTER SURGERY

Time of instituting ambulation after operations

Procedure	*On recovery*	*Day of operation*	*First day after*	*Second day after*	*Third day after*	*Later*	*Replies*
Herniorrhaphy..	10	30	37	3	2	1	83
Splenectomy....	2	8	52	12	5		79
Cholecystectomy	4	10	52	7	4		77
Gastrectomy....	3	8	43	10	9		73
Hysterectomy...	4	11	47	8	1		71
Thoracoabdominal operations.	1	5	32	20	10	1	69
Ureterorenal operations....	3	3	39	15	7	1	68
Prostatectomy..	1	6	31	12	11	4	65
Abdominoperineal operations....	2	4	20	19		18	63
Lung resection..	1	2	31	17	10	1	62
Removal of herniated nucleus pulposus (hemilaminectomy)....	1	3	12	11	12	14	53

Note: Figures given in table represent number of hospitals (not surgeons) and indicate the earliest time given for that hospital, although some members of the staff may begin ambulation later.

DISCUSSION

Since there is practically unanimous agreement both by those who use ambulation immediately, and those who use it very late, that postoperative walking causes no ill effects, and that it hastens recovery, and since many also believe that it prevents postoperative pneumonia and pulmonary embolism, the reluctance to have patients ambulate immediately, or on the day of operation, is indeed surprising. The discrepancies, inconsistencies, and conservatism provide convincing evidence that the rationale and therapeutic effect of early ambulation are not yet appreciated by the majority of surgeons in the United States.

The failure of surgeons to use ambulation promptly and aggressively suggests that there is a lingering reluctance to break with the teachings and practices of the past, as well as a lack of complete comprehension of the physiologic principles involved (3). There is no longer any question that patients should be encouraged to walk early after operation, instead of being confined to bed for 10 to 14 days, according to the traditional practice. The problems that remain regarding early ambulation involve the general acceptance of a more precise and methodical technique of administering this procedure so as to derive the maximum benefit from it. A more effective practice of early ambulation will evolve when the physiologic principles on which it is based are better understood. For this reason, it seems apropos to restate briefly the pertinent facts regarding the disruption of normal function by

surgical trauma, and to demonstrate how this disruption causing biologic imbalance may be alleviated promptly by walking.

HOMEOSTASIS

The primary function of involuntary muscles is to distribute vital body fluids wherever needed. This function is performed in synchronization with the heart action and the action of voluntary muscles. This involuntary muscular function is regulated largely by reflex action, through the mechanism of the sympathetic and parasympathetic divisions of the autonomic nervous system which activates or inhibits glands and involuntary muscles to meet shifting body requirements. The adrenal and pituitary glands act as governing pilots in this process, responding to each need as it arises. It is through this mechanism that groups of involuntary muscles are kept in optimal tonus and synchronized functional activity to deliver oxygen, electrolytes, and nutriments wherever and whenever they are needed.

DEVELOPMENT OF THE TRAUMA SYNDROME

According to the Arndt-Schulz law, physiologic activity is increased by weak or normal stimuli, and inhibited or abolished by very strong stimuli. The stimuli resulting from major surgical trauma are of such magnitude that they overactivate or overinhibit groups of involuntary muscles, particularly those of the intestinal tract, diaphragm, and peripheral vascular system. This is an inherent phase of the acute reaction to stress, as described by Selye. The overactivation or overinhibition of these special groups of muscles, initiated by surgical trauma, has a tendency to cause intestinal distention, contraction of the lungs, peripheral vasodilatation in the area of trauma, and peripheral vasoconstriction in remote areas. The result is a sluggish circulation.

Another result of trauma is that red blood cells become covered with a "sticky protein substance" which causes cohesion of these cells, to form microscopic "sludge"; some sludge is present after every operation, according to Knisely and associates. The sticky sludge is also likely to become attached to the walls of the veins, especially when circulation is sluggish, to form thrombi, most frequently in the veins of the legs. Confinement to bed intensifies the circulatory stagnation. Baker and Sedwitz have demonstrated that diodrast injected into the veins of the legs will remain visible by x-ray as long as 15 minutes when the subject is lying still, but movement of the leg muscles, such as flexion of the knee or wiggling the toes, immediately whips up the circulation so that the dye disappears into the general circulation. Thus a stagnant circulation is fertile soil for the development of loosely attached thrombi, which in some cases lead to pulmonary embolism.

Paralysis of the intestinal musculature and of the diaphragm which result, respectively, in intestinal distention and pulmonary deflation may complicate the trauma syndrome, and also contribute to further circulatory stagnation.

RATIONALE OF EARLY AMBULATION

Surgical illness, then, is brought about by powerful stimuli, resulting from trauma, which tend to inhibit function and thereby produce a sluggish circulation. This circulatory insufficiency, which is prolonged and intensified by constant confinement to bed, is the primary factor in the development of the adverse biologic changes that occur after surgery. For this reason, the pathologic functional changes following surgery should be reversed before severe metabolic imbalances occur.

Walking has a tendency to reverse the pathologic physiology by instituting substitution reflexes which whip up pulmonary ventilation and the general circulation. Voluntary contraction of large leg muscles shunts the sluggish venous blood into the arterial system. If this rationale is correct, then ambulation should be instituted immediately on recovery from anesthesia, especially in patients with severe manifestations of the trauma syndrome. Some of the most dramatic results in my own experience have been in patients that the majority of surgeons, judging from information furnished in the questionnaire, would regard as "too ill" to be subjected to immediate ambulation.

"Shock," internal hemorrhage, a recent coronary attack, and "hypovolemia" are recognized contraindications to immediate ambulation; these were mentioned frequently in the survey. A patient in true shock, with an ashen cyanosis, cold clammy skin, and peripheral vascular failure is too weak even to attempt ambulation, but if the condition is still reversible, then vigorous leg exercises, passive or active, may be of great value in stimulating circulation, and can be followed when the patient's condition warrants it, by judicious ambulation. A recent coronary attack is not necessarily an absolute contraindication,

but caution should be exercised in prescribing ambulation for any patient with such a history. In cases of true hypovolemia, blood volume must be restored by transfusion or intravenous fluids before ambulation is attempted. It should be noted, however, that in some cases, blood volume is adequate but is not circulating properly, because of venous stagnation resulting from the effects of trauma. In instances of this type, the arterial pressure may show a satisfactory increase after the first ambulatory period.

In our own practice (4), over 99 per cent of surgical patients get out of bed to walk, immediately after recovery from anesthesia. Delay in instituting ambulation is very rare, even after the most formidable procedures, such as gastrectomy, abdominoperineal resection, and even total pancreatectomy. The replies to the questionnaire indicate that many surgeons withhold ambulation from 1 to several days after these more serious operations. Yet these patients are the ones who would obtain the greatest benefit and would demonstrate the most striking results of immediate ambulation. In some such cases that we have observed, in which there was a striking reversal of apparent circulatory stagnation, early ambulation seemed to constitute a life-saving measure.

In these serious cases, of course, the surgeon himself, or a specially trained assistant, should supervise the first ambulatory period. An inexperienced nurse does not have the requisite skill and confidence to handle the mobilization of such patients.

EFFECTIVE REGIMEN OF EARLY AMBULATION

The significance of how early, how often, and how consistently postoperative walking should be prescribed is not yet sufficiently appreciated by many American surgeons, as is revealed by the present survey. If our concept of the pathophysiology of the trauma syndrome which follows surgery is correct, then the time, frequency, and vigor with which ambulation should be carried out assume great importance. Walking is a stabilizer of circulation. It accelerates and ventilates the general blood stream and has a tendency to promote homeostasis. In our experience, which includes random preliminary observations dating back to 1932, and continuous methodical clinical investigation and routine use of the procedure since 1938, the best results are obtained when ambulation is administered radically. This means that the surgical patient is routinely required to get up to walk immediately on recovery from the anesthetic. If he shows signs of fear or is reluctant to co-operate, 2 or 3 ambulatory periods in rapid succession are very effective in overcoming the difficulty. Directing the patient to walk up and down a flight of stairs, or to do bending exercises, also alleviates fear rapidly. Usually a patient should be required to walk once every hour during the first 4 hours after recovery from the anesthetic. By the following day, most patients require little or no supervision, except the constant reminder to walk frequently. Patients will not be too active, no matter how much prodding they receive. With this regimen, narcotics should be employed very sparingly, after operation.

When ambulatory treatment is properly understood, it is the surgeon's responsibility and not the patient's desire which should regulate the time, frequency, and consistent requirement of postoperative walking, in accordance with the patient's needs.

SUMMARY

The replies received to a questionnaire on present practices with regard to early ambulation after surgery in University and private hospitals throughout the United States indicate that the idea of this procedure has been universally accepted, but that the principles and rationale are as yet incompletely understood. There is no longer any doubt that patients should not be confined to bed for prolonged periods after operation. Nevertheless, only a small minority of surgeons practice early ambulation in a way that will be of most benefit, considered in the light of the pathophysiology of the trauma syndrome. The great majority still fail to employ ambulation early enough after recovery from the anesthetic and with sufficient frequency during the immediate postoperative period to counteract effectively the impairment of circulatory, pulmonary, and digestive function resulting from the operation.

It is hoped that the present re-emphasis on the rationale of early ambulation will persuade those who believe they are using ambulation effectively after surgery, to examine their present practices in the light of principle. The present survey demonstrates that judicious ambulation, when vigorously applied, causes no ill effects to the surgical patient. The 5 instances of "com-

plications" cited in the questionnaires were by individual surgeons who do not use immediate ambulation, but get their patients out of bed from the second to the fifth day after operation. The opinion by surgeons who use ambulation on recovery from anesthesia, or on the day of operation is practically unanimous that it hastens recovery and prevents postoperative pneumonia and pulmonary embolism.

When the rationale of ambulatory treatment is properly understood, many so-called "contraindications" become primary indications for vigorous insistence on early and frequent ambulation during the immediate postoperative period. With such an evaluation, it is the surgeon's responsibility, and not the patient's desire, which regulates the time, frequency, and consistent requirement of postoperative walking, in accordance with the patient's needs.

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A NEW APPROACH TO THE SURGICAL MANAGEMENT OF PEPTIC ULCER BY GASTRECTOPLASTY

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In 1885, only 4 short years after Billroth (10) performed the first successful gastrectomy, he abandoned the technique in favor of a second method, subtotal gastrectomy with gastrojejunostomy. This Billroth II procedure was thought to obviate the major failings of the Billroth I method; that is, stenosis and anastomotic leak at the "fatal angle" due to excessive tension on the suture line connecting the gastric pouch to the duodenum. Variations of the Billroth II procedure have withstood the test of time and the vicissitudes of the popular medical opinion until today it stands as one of the most commonly accepted surgical approaches to peptic ulcer and gastric cancer.

As early as 1925, Morley (22, 23) believed that gastroduodenostomy was the more physiologic method of reconstruction following partial gastrectomy. He thought that the Polya-Billroth II operation carried a marked tendency toward postoperative anemia. More recently, Everson (5, 6), Harkins and associates, Moore and Harkins, and others have seriously challenged the position of the second Billroth procedure and have re-examined the place of the Billroth I operation. These investigators suggest that exclusion of the duodenum may have serious implications in the efficiency of digestion and absorption.

The voluminous contributions directed toward alleviation of the problems of the Billroth I gastrectomy may be divided into several categories. The first group consists of variations in the gastroduodenal anastomosis. The original end-to-end anastomosis of Péan, Rydygier, and Billroth was changed to a side-to-end closure by Kocher (16) in 1893. The gastric pouch was completely closed and an anastomosis was made between an opening in the posterior wall of the stomach and the end of the duodenum in order to eliminate the so-called fatal angle. Haberer (8) in 1922, and Finney independently, in 1923, proposed an anastomosis of the greater curvature aspect of the gastric remnant to the side of the duodenum (end-to-side or terminolateral gastroduodenostomy).

A second group of concepts was concerned with equalizing the size of the gastric and duodenal stoma. In 1889, Eiselsberg modified the second Billroth procedure by partially closing the gastric pouch and leaving a smaller stoma for anastomosis with the jejunum. Hofmeister, in 1896, resected wider amounts of the lesser curvature and like Eiselsberg, partially closed the gastric pouch except for a small stoma at the greater curvature aspect. Schoemaker expanded this principle in 1911, but united the gastric stoma directly to the duodenum. In 1923, Mayo placed extra stitches in the stomach to equalize the two openings and Haberer (9) pleated the stomach on the duodenum. Horsley split the anterior wall of the duodenum longitudinally to increase the size of the duodenal orifice.

A third group of procedures proposed eliminating the gastroduodenal anastomosis entirely by retaining the gastric antrum. Connell experimentally (1) and clinically (2) resected the fundus of the stomach but preserved the pylorus and antrum. He believed that this technique would produce achlorhydria as well as eliminate dumping. Wangensteen (27), in 1940, described a variant of Connell's fundusectomy which he called tubular resection with a transverse gastroplasty. After resection of the fundus (75 per cent gastrectomy), the antrum was sutured to the cardia by using a transverse closure. In a follow-up study Wangensteen and his coworkers (16) also described a method by which the mucosa was peeled off a portion of the remaining lesser curvature. Proximal subtotal gastrectomy, in which the cardia and fundus

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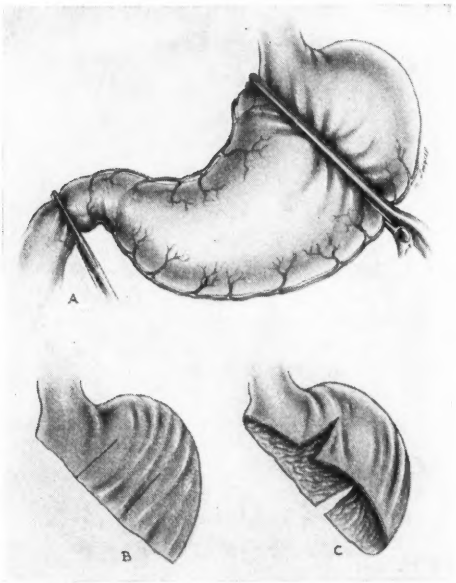

FIG. 1. A, Subtotal gastric resection. B, Lines of proposed incision on anterior and posterior walls. C, Incisions into gastric pouch.

were excised and the remaining antrum united to the esophagus, has been proposed. Wangensteen (3, 28) in 1951 revived the segmental resection previously reported by Mikulicz; he used an extensive (75 per cent) segmental resection with anastomosis of the antrum to the cardia.

A fourth group of contributions centers about ways and means of mobilizing the organs for easier anastomosis. The first, and one of the most significant, of these methods was proposed by Kocher (17) in 1903. He incised the peritoneum lateral to the second portion of the duodenum and found he could gain considerable length and mobility of this organ. The wider gastric resections advocated in more recent years by Wangensteen (29) and others have intensified the search for more effective measures of mobilization. Techniques used to mobilize the gastric pouch include: incision of the gastrophrenic and gastrolienal attachments, incision of the esophagophrenic ligament, and mobilization of the distal esophagus. Furthermore, it has been suggested that the cystic duct be severed (with subsequent cholecystectomy) in order to gain more mobility for the common duct and duodenum. Notwithstanding, there may be instances in which mobilization fails to achieve sufficient length for comfortable anastomosis. Utilizing a concept previously developed by Hunnicutt and Longmire and Beal, Moroney has suggested an operation using a transverse colonic segment for bridging the gap between the gastric pouch and the duodenum. Henley described a similar technique using jejunal segments. Both of these techniques have been proposed as primary gastrectomy procedures as well as for the conversion of the Billroth II to the Billroth I type of repair.

A previous report (26) from this laboratory described methods of managing the gastric remnant following high subtotal gastrectomy to facilitate gastroduodenostomy in dogs. These methods dealt directly with the small gastric remnant by means of plastic procedures to lengthen this pouch in order to facilitate gastroduodenostomy. The present report describes the use and preliminary results of this technique in a series of 9 patients.

TECHNIQUE

The upper abdomen was opened in the midline; the xiphoid was split or excised to facilitate exposure when necessary. The stomach was mobilized in the usual manner, and a high subtotal gastrectomy was performed (Fig. 1A). Removal of 75 per cent, or more, of the stomach was strived for and usually attained. The duodenum was mobilized, clamped, and severed 2 or 3 centimeters distal to the pylorus. Except for the narrow margin necessary for suture lines, all of the lesser curvature was included in the resection. The resection was carried to a point approximately halfway through the vasa brevia on the greater curvature. The lateral vascular omental attachments of the stomach to the diaphragm and kidney were severed. A Payr clamp was placed across the line of the proposed resection and the distal portion of the stomach excised (Fig. 1B).

Two staggered incisions approximately 6 to 8 centimeters in length were made in the remaining gastric pouch (Fig. 1B and C). The incision on the anterior wall was made at the junction of the upper and middle thirds; a similar incision was made in the posterior wall at the junction of the middle and lower thirds. Bleeding points were carefully controlled with plain

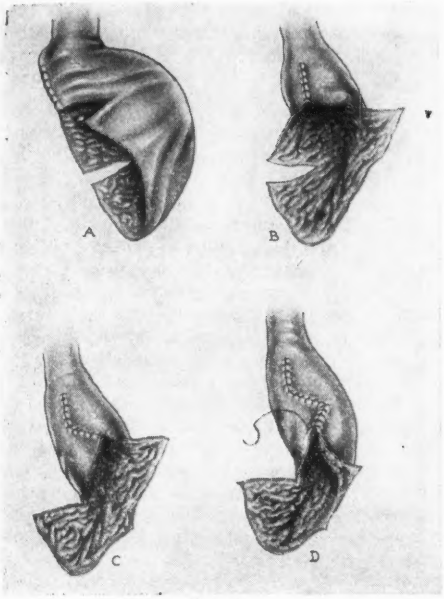

FIG. 2.

FIG. 2. A, Closure of upper third of gastric pouch. B, Flap of anterior wall formed by incision retracted laterally. C, Posterior wall flap united to anterior wall incision. D, Continuous suture being carried down to unite anterior wall flap to posterior wall incision.

FIG. 3. A, Anterior wall flap united to upper margin of posterior wall incision. B, Lower limb of modified Z completed. C, The gastric pouch is anastomosed to the duodenum.

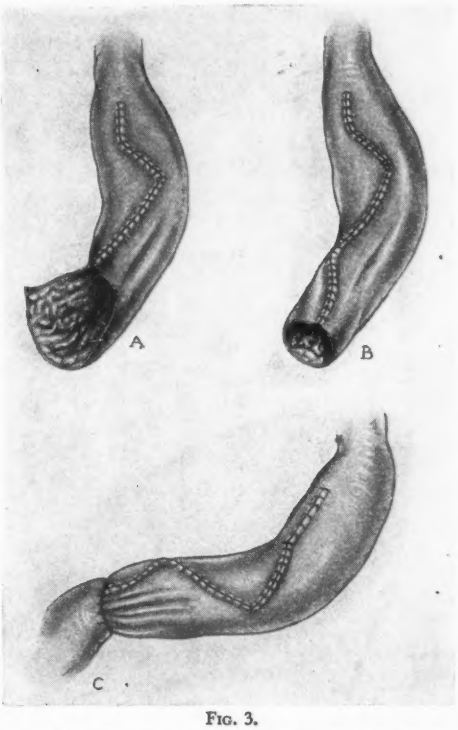

FIG. 3.

catgut ties. At the upper third of the pouch the anterior and posterior walls were closed with a continous inverting mattress suture (Fig. 2A). The flap of the anterior wall created by the incision was retracted laterally (Fig. 2B). The middle third of the posterior wall was then joined to the upper margin of the anterior wall incision by the continuous inverting suture line (Fig. 2C). This suture was continued downward to join the lower margin of the anterior wall incision to the upper margin of the posterior wall incision as in a modified Z-plasty (Fig. 2a and 3a). As the final limb of the Z was completed (Fig. 3b) the cylindrical or tubular appearance of the gastric pouch became more evident. A second layer of interrupted silk mattress sutures was employed in order to reinforce the closure which had been made.

The increased length of the lesser curvature aspect of the gastric pouch allowed anastomosis with the duodenum without undue strain or tension. Two layers of interrupted mattress sutures were used for the gastroduodenostomy (Fig. 3c). A Levin tube was left in place in the stomach in order to provide for continuous postoperative suction.

RESULTS

This technique has been performed on a series of 9 patients; 8 patients had peptic ulcer (5 duodenal, 3 gastric), and 1 patient had carcinoma of the stomach. In 1 instance the patient had a complicating pyloric obstruction from a previous perforation, 1 patient had recurrent episodes of melena and 4 patients had massive upper gastrointestinal hemorrhage from peptic ulcer (2 gastric, 2 duodenal), 1 patient had advanced antral carcinoma with pyloric obstruction and lymph node metastases, and 2 had intractable duodenal ulcers. There have been no deaths and no unusual consequences. The patients have been followed-up for a period of from

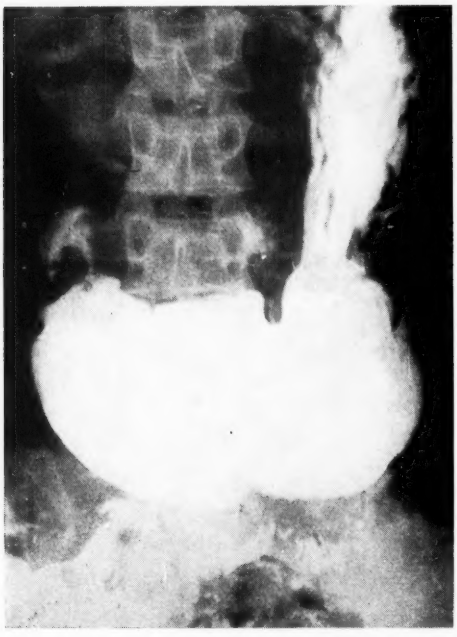

FIG. 4. Case 1. Roentgenogram showing large dilated stomach with pyloric stenosis.

2 months to 1 year. All patients have been achlorhydric postoperatively except 1 who had 15 clinical units of free acid after histamine. Roentgenograms of the gastrointestinal tract have demonstrated satisfactory function. Thus far, there has been no evidence of nutritional difficulties or failure to maintain weight. The following are illustrative cases:

CASE 1. N. W., a 25 year old colored male, was admitted to Hahnemann Hospital on August 30, 1955. Three weeks previously he had a perforated (postpyloric) duodenal ulcer; the perforation was closed without incident. Two weeks after this procedure a rather sudden exacerbation of the ulcer symptoms developed with persistent vomiting. Roentgenograms at this time showed almost complete pyloric obstruction (Fig. 4). After preoperative preparation gastrectoplasty was performed although at least 85 per cent of the stomach was removed, including the entirety of the lesser curvature, gastroduodenal anastomosis was rather easily performed. The postoperative course was uneventful. Roentgenograms of the gastrointestinal tract taken 2 and 6 months after the operation showed a satisfactory functioning gastric remnant and gastroduodenal stoma, with prompt but not unduly rapid gastric emptying (Fig. 5).

CASE 2. A. G., a 56 year old white male, was admitted on December 28, 1956 with a massive upper gastrointestinal hemorrhage. He gave a history of heavy wine consumption for the past 10 years. Six

FIG. 5. Postoperative films in Case 1 showing outline of reconstructed gastric remnant. Left, Anteroposterior view; right, an oblique view showing the lateral silhouette.

days prior to admission he noted severe epigastric pain and melena. In spite of 4,500 cubic centimeters of whole blood replacement in the first 36 hours after admission the hemoglobin fell from 10 to 8.8 while the hematocrit remained close to 33. At operation a large gastric ulcer was found on the lesser curvature close to the esophagogastric junction. Seventy-five per cent of the stomach was removed; it was necessary to take the lesser curvature to within 1 or 1½ centimeters from the cardioesophageal junction. A gastrectoplasty allowed fairly easy performance of a gastroduodenostomy. Recovery was uneventful, and the patient has remained in good health since operation.

CASE 3. W. N., a 72 year old negro male, was admitted on January 12, 1956. He gave a 2 weeks' history of vomiting after each meal, associated with epigastric distress and distention. He was asthenic, moderately dehydrated, and in relatively poor nutritional status. There was a nontender, movable mass palpable in the mid-epigastrium. Roentgenograms revealed a prepyloric lesion with pyloric obstruction. On abdominal exploration, an advanced gastric cancer was found with almost complete pyloric obstruction, and lymph node involvement in the subpyloric, preaortic, and midcolic areas. A palliative resection was carried out in which 4 or 5 centimeters of the duodenum and at least 75 per cent of the stomach including most of the lesser curvature were removed. The patient did remarkably well postoperatively, and when last seen, 6 months after the operation, he was still maintaining his weight to within a few pounds of what it was preoperatively.

DISCUSSION

Some 37 or more operations for subtotal removal of the stomach have been proposed since Péan, Rydygier, and Billroth's first attempts. Many of these procedures have been concerned with variations and modifications of the manner in which the gastric remnant was attached to the jejunum or duodenum; that is, isoperistaltic, antiperistaltic, antecolic, postcolic, Hofmeister, end-to-side, side-to-end, and end-to-end. A number have been concerned with ways and means of mobilizing the duodenum and the gastric remnant for gastroduodenostomy. We believe the procedure introduced is the first attempt to deal directly with the gastric pouch remaining after high subtotal gastrectomy; an attempt is made to lengthen this pouch by means of plastic procedures so that effortless gastroduodenostomy may be attained. We hope that with this introduced concept one need not resort to performing less than an adequate gastrectomy in order to permit gastroduodenal closure.

We have referred to this technique as a gastrectoplasty, a plastic procedure on the gastric remnant following subtotal gastrectomy.

SUMMARY

A technique of management of the small gastric pouch for gastroduodenostomy after high subtotal gastrectomy is presented along with the preliminary results in a small series of cases.

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STUDIES IN EXTRACORPOREAL CIRCULATION

IV. Surgical Techniques

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WHEN OPEN INTRACARDIAC OPERATIONS are made possible by wholly maintaining the systemic circulation with a mechanical pump-oxygenator, there is of necessity diversion of venous blood from the subject to the apparatus and return of oxygenated blood from the apparatus to the subject. If a perfusion flow approaching the resting cardiac output of the subject is desired, a technique must be employed that allows rapid transport and oxygenation of large quantities of blood without deleterious effects. Although during perfusion the heart is functionally excluded from the systemic circulation, blood enters the myocardium through the coronary arteries and drains in normal fashion to the cardiac chambers. If induced cardiac asystole is employed, coronary circulation is interrupted during the period of asystole, but bronchial flow to the lungs continues and reaches the heart by way of the left atrium or by retrograde flow through the pulmonary artery into the right ventricle. Provision must be made, therefore, for removal of this blood in such a manner that it need not be discarded but can be readmitted to the general circulation. The surgical techniques for directing large flows of blood from and to the subject and of handling the intracardiac return are thus part of the general problem of extracorporeal maintenance of the circulation during open intracardiac operations.

The method of handling the intracardiac return during open cardiotomy has been reported (1). Herein will be described the surgical techniques and equipment used to establish, maintain, and conclude extracorporeal circulation.

PRELIMINARY PREPARATIONS

During the period of extracorporeal circulation the operating room with personnel and equipment is arranged as illustrated in Figure 1. The pump-oxygenator which we use (3) is prepared and brought to the operating room after the operation is under way, but in adequate time to fill it with blood and establish a blood film over the oxygenator screens. The cannula systems are prepared and assembled by a surgically sterile assistant in an adjoining area while the incision is being made.

The operating table is put into position at a standard height with the level of the right atrium approximating the level of the venous reservoir in order to minimize the effect of gravity on the flow of blood from the venae cavae. The table is also covered with a Bigelow hypothermia blanket, the heating element of which is used for warming the patient to counteract loss of heat from the blood during the period of extracorporeal circulation. Padding is placed under bony prominences to avoid burning.

After the patient has been weighed carefully, he is brought to the operating room and anesthetized. The anesthesiologist places the electroencephalographic and electrocardiographic electrodes, introduces the rectal thermometer, and does the necessary venous punctures. The surgeon introduces a fine catheter into the aorta through a needle inserted percutaneously into the right femoral artery. This is attached to a strain-gauge manometer for monitoring aortic blood pressure. A catheter is introduced into the inferior vena cava through the left saphenous vein. For this procedure a small incision is made over the saphenous vein in the left groin, and the vein is dissected free and ligated distally. A polyethylene catheter corresponding in size to a 16 or 18 gauge needle is placed in the saphenous vein and passed into the lower part of the inferior vena cava for the purpose of measuring central venous pressure. The percutaneously introduced aortic catheter is removed at the end of

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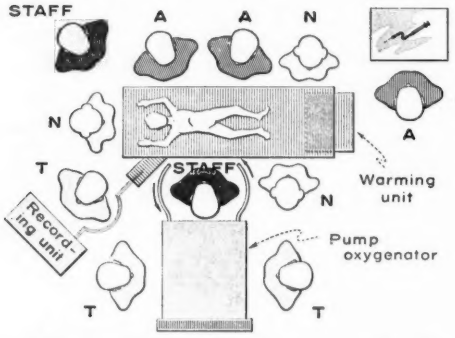


FIG. 1. Arrangement of operating room during extracorporeal circulation procedure. *Staff* refers to permanent professional staff of the clinic, including the surgeon and the anesthesiologist. Surgical assistants are indicated by *A*, 2 of whom assist with the operation throughout and the third prepares special equipment such as cannulas and the potassium-blood mixture for elective cardiac arrest. Three nurses, indicated by *N*, include the nurse anesthetist and 2 surgical nurses. Two technicians (*T*) operate the pump-oxygenator and the third technician records physiologic data.

the procedure without ligation of the artery. The catheter in the vena cava is left in place for 24 to 48 hours for the intermittent measurement of central venous pressure and for the administration of blood and fluids.

INCISION OF THORAX

In open intracardiac operations with extracorporeal circulation, it seems desirable for the surgeon to have access to both pleural cavities for the necessary cannulation procedures and for adequate exploration of the heart and great vessels. This exploration can be accomplished best through a bilateral intercostal incision and transverse sternotomy. The fourth interspace is the most frequently used (Fig. 2), although the configuration of the thorax or the nature of the cardiac lesion present may dictate the use of either the third or the fifth intercostal space. A submammary incision of the skin is made from the posterior axillary line over the appropriate interspace to the corresponding area on the opposite side. After both pleural cavities have been entered and the internal mammary vessels have been dissected free, the sternum is transected in a V shaped fashion in order to increase stability at the time of closure. After the sternum is transected, the internal mammary vessels can be easily divided and ligated. Superiorly, the thymus is dissected free to gain exposure of the base of the heart and the great vessels.

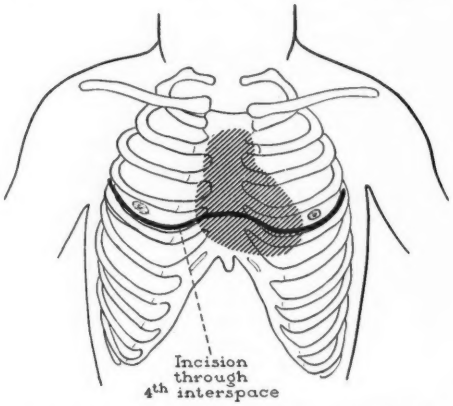


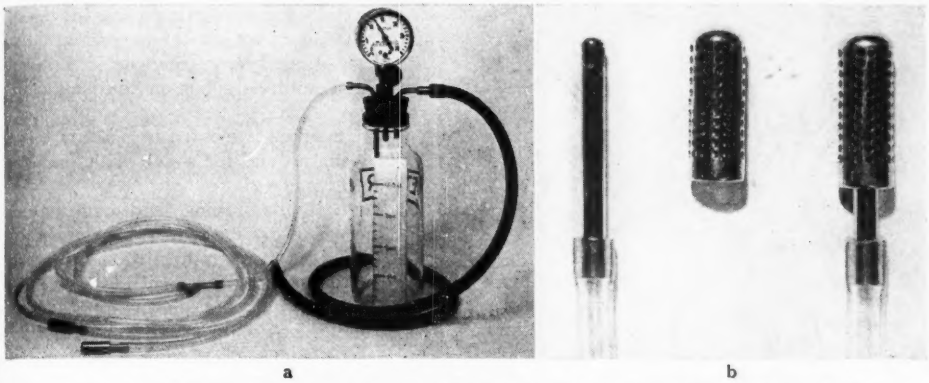
FIG. 2. Incision of the thorax through the fourth intercostal space, transecting the sternum.

DRAINAGE OF THORAX

Since it is desirable to maintain the blood volume as constant as possible during the period of extracorporeal circulation, the blood lost must be replaced minute by minute as the loss occurs. The major portion of this loss occurs within the thoracic cavity, and if provision is made for measuring this loss as it occurs the problem of blood replacement is simplified. Therefore, a drainage tube is placed through a stab wound in the thoracic wall into the gutter of each cavity and connected to a graduated suction bottle in which the negative pressure is maintained at 15 millimeters of mercury (Fig. 3a). Perforated metal guards are attached to the ends of the polyvinyl (tygon) tubes (Fig. 3b) to allow continuous drainage and to protect the lung from being sucked into the end of the tube. The guards are easily removed at the end of the procedure, the polyvinyl tube is withdrawn, and the usual drainage catheter is placed through the same stab wound.

ARTERIAL AND VENOUS CANNULATION

The following characteristics have been found desirable in a system of tubes and cannulas designed to handle relatively high flows in subjects differing greatly in size: (1) The system must be such that it is easily cleaned, sterilized, and



a b

FIG. 3. a, Thoracic suction apparatus for collection of blood during operation. The heavy black tube is connected to the regular suction line, and the negative pressure within the graduated collecting bottle is regulated by means of the valve in the stopper. The polyvinyl tubes lead to the thorax, 1 for each side. b, Metal guards for drainage of the thorax. The outer perforated guard is easily removed.

assembled. (2) The system must minimize trauma of the blood. (3) There must be a range of cannula sizes to accommodate the flows encountered and the vessels to be cannulated in patients of different ages and sizes. (4) Junctions and connections should be of standard pattern and easily interchangeable to facilitate selection of the optimal cannula size at the operating table. (5) The cannulation systems should not unduly incommode the surgeon during the intracardiac procedure. (6) The various cannulas should be easy to insert securely into their respective vessels. (7) Expulsion of air from the entire system should require a minimum of time and blood. (8) Secure fittings must be obtained at the various junctions and connections to avoid disastrous disconnections, particularly in the high pressure lines.

Arterial cannulation system. Oxygenated blood is returned to the subject via a cannula placed in the aorta through the previously divided left subclavian artery. A single arterial flow line of polyvinyl (tygon) tubing with an internal diameter of ½ inch connects the "arterial" side of the pump-oxygenator to the cannula system proper.

The arterial cannulation system consists of a stainless steel L-shaped cannula, an 18 inch length of polyvinyl tubing, and a stainless steel adapter (Fig. 4). The foot of the cannula is beveled at 60 degrees, and a small ridge is placed 1.5 centimeters back from the grooved head. The shank of the cannula ends in a grooved adapter head. Cannulas with an internal diameter of 2.3 through 5.4 millimeters have heads which fit polyvinyl tubing with an internal diameter of 4/16 inch, while cannulas with an internal diameter of 6.4 through 7.0 millimeters have heads which fit 5/16 inch tubing. When assembled for use, a heavy ligature is placed around the tubing below the grooved connector head as a further precaution against the cannula's pulling free from the tubing (Fig. 5).

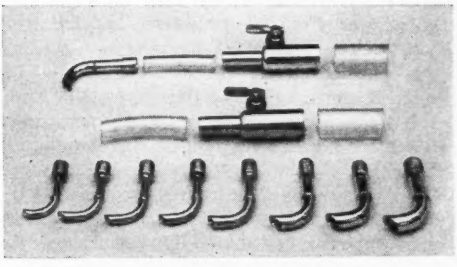


FIG. 4. The arterial cannula assembly. At the top, from left to right, are the subclavian artery cannula, polyvinyl tube with an internal diameter of ¼ inch (actual tube is longer than shown here), arterial adapter with stopcock for removal of air, and polyvinyl tube with an internal diameter of ½ inch which attaches to the pump-oxygenator. In the center is shown the arterial adapter for uniting 5/16 inch tubing with ½ inch tubing. At the bottom are various sizes of arterial cannulas, all of which fit the ¼ inch adapter except the one on the right which fits the 5/16 inch adapter.

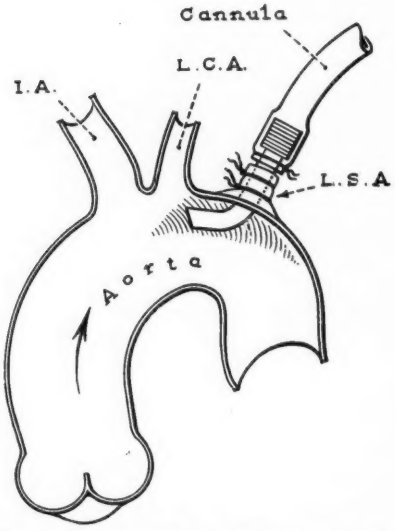


FIG. 5. Representation of the relationship of the arterial cannula to the aorta.

Two adapters are provided, one to unite the 4/16 inch tubing with the ½ inch tubing of the main arterial flow line, and the other for use with the 5/16 inch tubing. The junction between the large and small tubes of the adapter takes the form of a gentle slope. A stopcock fitted to the larger tube of the adapter allows air to be easily withdrawn from the system prior to the beginning of perfusion.

Technique of arterial cannulation. The following steps are used in this technique:

1. The left subclavian artery is isolated between its aortic origin and its first major branches, divided between ligatures, and brought down to a more convenient position for cannulation (Fig. 5).

2. A heavy silk ligature is passed around the aortic end of the artery and a noose is formed by passing the free ends of the ligature through the eye of an aneurysm needle.

3. The noose is tightened to occlude the artery and a longitudinal slit is made through the vessel wall some 1.5 centimeters from the aortic origin.

4. The arterial cannula is then introduced into the lumen of the artery, the noose being momentarily loosened to permit the passage of the cannula into the aorta, then tightened to prevent bleeding.

5. Once in the aorta the cannula is securely seated with its orifice pointing toward the aortic valve. Particular care is taken to ensure that the cannula is situated completely within the aortic lumen and not impinging on the wall of the vessel.

6. The cannula is secured in position by ties of heavy silk around the shank of the cannula, distal to the metal ring.

7. The cannula, tubing, and main arterial flow line which has been filled previously with blood are joined through the metal adapter, and the remaining air is withdrawn via the stopcock. The entire flow line between the apparatus and the aorta of the patient is now completely free of air.

Venous cannulation system. Cannulas placed in the inferior vena cava and the superior vena cava respectively serve to direct a flow of venous blood from the subject to the apparatus. A single main flow line of polyvinyl tubing with an internal diameter of ½ inch connects the venous cannulas to the "venous" side of the mechanical pump-oxygenator.

The cannulas (Fig. 6) consist of polyvinyl tubes 18 inches long which may be cut to the length desired after insertion. The cannula for the superior vena cava is molded by heat into an L shape with an angle of about 60 degrees

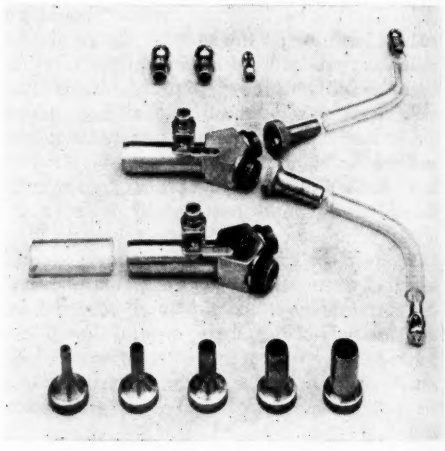


FIG. 6. The venous cannula assembly. At the top are metal heads which fit into the ends of the polyvinyl tubing placed in the venae cavae. In the middle are 2 of the connections that adapt the 2 venous cannulas to the main venous line to the pump-oxygenator. Below are the inlet arms that are used for adaptation to various sizes of cannulas used.

between the two limbs to facilitate introduction of the cannula as well as to afford better positioning within the cava. The small open-sided metal head that rests within the cava functions principally to give a smooth, rounded surface to facilitate introduction. A metal connector consisting of two inlet arms that are interchangeable for various sized cannulas and a single arm with an internal diameter of ½ inch joins the two vena caval cannulas with the single line that leads to the pump-oxygenator. The two inlet tubes of the connector have standard-sized threaded heads which screw into the chamber of the connector, a leak-free union being assured by a rubber-ring seal. Inlet tubes of different internal diameters are provided and thus combinations of venous cannula sizes may be obtained with the same connector. The connector is fitted with a stopcock which permits air to be readily aspirated from the system prior to the beginning of the perfusion.

Technique of venous cannulation. The following steps are practiced in establishing an air-free venous flow line between the patient and the apparatus:

1. The single venous flow line between the patient and the pump-oxygenator is filled with blood from the apparatus prior to commencement of cannulation of the great veins (Fig. 7).

2. The right atrium and the right ventricle are widely exposed through a curved incision in the pericardium over the base of the heart with reflection of the pericardium caudad. Umbilical tapes are passed doubly around the inferior vena cava and the superior vena cava with the free ends of the tapes being threaded through short lengths of rubber tubing for occlusion of the respective veins at the appropriate time.

3. The right atrial appendage is clamped with a Glover clamp, and a Rummel tourniquet is placed on the cardiac side of the clamp.

4. The right atrial chamber is then examined with a finger which is inserted through an incision in the right atrial appendage. Upon completion of the intracardiac exploration, the Rummel tourniquet is tightened as the exploring finger is withdrawn.

5. The inferior vena caval cannula is introduced into the right atrial cavity through this incision as the Rummel tourniquet is loosened and then again tightened around the cannula. The cannula is guided into the inferior vena cava a distance of 3 or 4 inches and then withdrawn 2 or 3 inches leaving approximately 1 inch of the cannula within the cava. Difficulty in getting it to advance in the cava may indicate that the head of the cannula is entering a hepatic vein rather than the cava.

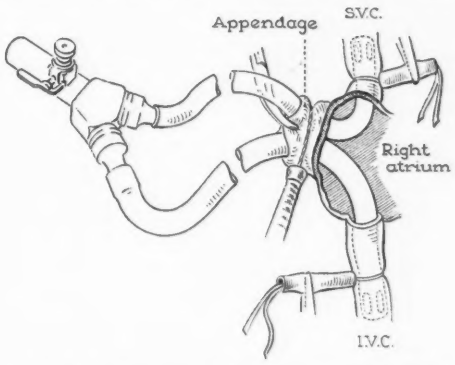


FIG. 7. Representation of the venous cannulas placed into the superior vena cava and the inferior vena cava through the right atrial appendage.

6. The superior vena caval cannula is inserted in a similar manner through the same incision in the atrial appendage.

7. A small curved hemostat is placed across the lips of the single atrial wound between the two cannulas, thus snugly approximating the lips of the incision about each tube. This maneuver plus the firm clasp of the Rummel tourniquet serves to avoid loss of blood until the tapes can be tightened about the cannula in the caval veins as the extracorporeal circulation is initiated.

8. The caval cannulas and the main venous line to the apparatus are now joined through the metal connector and the remaining air is removed from the flow lines with a syringe attached to the stopcock of the connector.

General considerations in cannulation. In order to reduce to a minimum the trauma occasioned by passing blood over a "foreign" surface, the interiors of all metal tubes and connectors are highly polished, thus obviating the necessity to use silicones, and junctions between tubes of different sizes are made gradually, not in abrupt fashion. Bends and angles are avoided wherever possible. Velocity of flow and resistance to flow are reduced by the use of polyvinyl tubing of large internal diameter. Therefore, the flow lines between the patient and the apparatus and

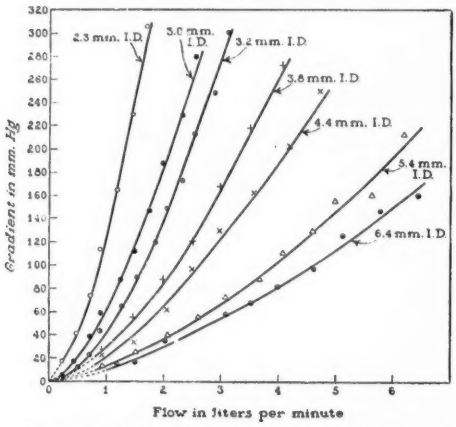


FIG. 8. Graph of resistance across the arterial cannula assembly (subclavian cannula, ¼ inch polyvinyl tube, and arterial adapter) at different rates of flow.

within the pump-oxygenator itself are of tubing with an internal diameter of ½ inch, the smaller tubing serving only as a connector, the length of which can be kept to a minimum.

Since the entire arterial return to the patient is made through a single cannula, and since it is preferable to avoid forcing blood at high pressure through a narrow orifice, the actual cannula used is the largest that can be introduced through the subclavian artery of the particular patient. It has been unnecessary to use a cannula of larger size than 6.4 millimeters even for adult patients. Figure 8 presents a graph in which pressure has been plotted against flow for the sizes of cannulas in use and emphasizes the desirability of using a cannula of maximal internal diameter. Table I lists the cannula sizes used in clinical work with patients differing considerably in body weight.

TABLE I.—SIZES OF ARTERIAL AND VENOUS CANNULAS FOR PATIENTS OF DIFFERENT WEIGHTS

Weight of patient		*Size of catheter*					
		*Arterial**		*Venous†*			
				Usual		*Range*	
Pounds	*Kilograms*	*Usual*	*Range*	*SVC*	*IVC*	*SVC*	*IVC*
5– 13	2.3– 5.9	3.0	2.3–3.8	2‡	2‡	2–3	2–4
13– 20	5.9– 9.1	3.2	3.0–4.4	2	2	2–3	2–4
20– 32	9.1–14.5	3.4	3.0–4.4	2	2	2–3	2–4
32– 50	14.5–22.7	3.8	3.2–4.9	2	3	2–4	2–4
50– 75	22.7–34.0	4.4	3.4–5.4	3	3	2–4	2–5
75–120	34.0–54.4	4.9	3.8–5.9	3	4	2–4	3–5
120–140	54.4–63.5	5.4	4.4–6.4	3	4	3–5	3–5
140–160	63.5–72.6	5.9	4.4–6.4	4	4	3–5	3–5
160–190	72.6–86.2	6.4	4.9–7.1	4	5	3–5	3–5
190+	86.2+	7.1	5.4–7.1	4	5	3–5	3–5

*Size is internal diameter measured in millimeters.
†Size number represents internal diameter in sixteenths of an inch.
‡Polyethylene catheters without metal heads are used occasionally for very small infants.

The same general principles apply to the selection of suitable venous cannulas, but here the problem is rendered less acute by the larger size of the vessels involved and the dual nature of the outflow system.

The incorporation of these features into the artificial vascular pathways causes relatively little damage to the blood as reflected in the low figures for hemolysis from actual perfusions. In clinical work, hemolysis has been consistently less than 40 milligrams per 100 cubic centimeters in samples taken just prior to the end of the perfusions, which have varied in length from 20 to 75 minutes.

INDUCED CARDIAC ASYSTOLE

As originally advocated by Melrose and co-workers and subsequently employed clinically by Effler and co-workers, the use of potassium to induce cardiac asystole makes possible more precise repair of most intracardiac defects. Therefore, this technique is used at present for most intracardiac operations requiring extracorporeal circulation.

Prior to cannulation, the ascending aorta is dissected free to allow cross clamping of it proximal to the innominate artery at the appropriate time. An umbilical tape is placed loosely around the aorta to aid in the subsequent application of the aortic clamp.

Potassium-blood mixture assembly. The mixture injected into the aorta to produce asystole is made by mixing 8 cubic centimeters of a 25 per cent solution of potassium citrate in 92 cubic centimeters of heparinized, oxygenated blood which is obtained from the arterial oxygenator line at the time the cannulation connections are being made. The assembly consists of two 30 cubic centimeter syringes attached to a three-way stopcock which is connected to a 19 gauge needle by means of plastic tubing some 15 inches long (Fig. 9). The length of tubing makes for better maneuverability of the needle without danger of tearing the aorta during the injection. Two smaller syringes and a three-way stopcock are used in preference to 1 large syringe to allow a more forceful and rapid injection with less danger of jamming the barrel of the syringe.

Induction of asystole. After extracorporeal circulation is initiated and it is apparent that the

perfusion is progressing satisfactorily, a Gross coarctation clamp is placed in position across the aorta at the site of the previously placed umbilical tape, the needle of the potassium-blood assembly is inserted in the aorta proximal to the clamp, and as the aorta is cross clamped the potassium-blood mixture is injected rapidly. The injection is made continuously until asystole occurs, at which time the amount injected is noted, and an additional 25 per cent is injected and the needle removed. Usually, 20 to 40 cubic centimeters of the solution is injected. One stitch of No. 5-0 silk is then placed to control bleeding from the needle puncture in the aorta.

Restoration of cardiac action. Upon completion of the intracardiac procedure the aortic clamp is removed, thus allowing resumption of coronary circulation and removal of the potassium from the coronary vessels. The first blood obtained from within the heart after release of the aortic clamp is aspirated and discarded. Resumption of cardiac action appears to be more satisfactorily accomplished when a relatively high perfusion flow is maintained, which results in better coronary circulation. Ventricular fibrillation may occur when cardiac action is resumed. If this does not revert to sinus rhythm spontaneously by the time the cardiac incision is closed, defibrillation is accomplished by the electric-shock defibrillator.

ATRIOTOMY AND VENTRICULOTOMY

The same general technique is followed in both procedures. On completion of cannulation, the perfusion is started, the tapes about the venae cavae are tightened so as to occlude the great veins about their respective cannulas, and asystole is induced if it is to be used. The atrium or the ventricle is opened through a generous incision. In both cases, the intracardiac return sucker is inserted to the most dependent portion as soon as the cardiac chamber is opened.

The right atrial incision extends across the full length of the lateral wall.

The right ventricular wound is made first in the outflow tract into the relatively avascular region which lies equidistant from the pulmonary valve and the anterior interventricular sulcus. Retraction sutures are placed in the wall of the ventricle lateral to the incision, which is extended freely to give adequate exposure but avoiding, if possible, major coronary vessels.

After the intracardiac procedure has been completed and cardiac action resumed, the closure of either an atrial or a ventricular wound is first effected by a continuous over-and-over suture, the intracardiac sucker being removed and the chamber allowed to fill with blood as the final stitches are inserted. The caval tapes are then released, the superior vena caval cannula is removed and the inferior vena caval cannula is withdrawn into the right atrium.

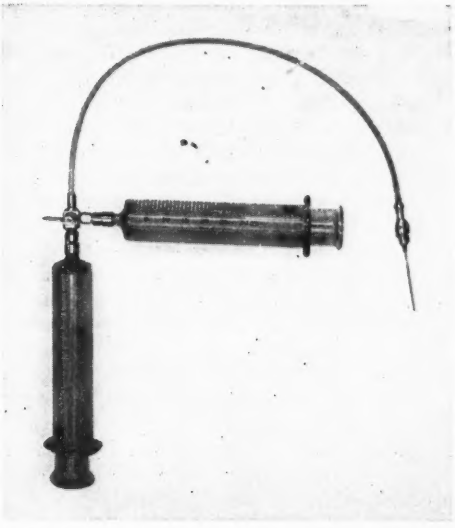


FIG. 9. Assembly for injection of potassium-blood mixture.

TERMINATION OF EXTRACORPOREAL CIRCULATION

With the cardiac incision closed by a single row of continuous sutures, the constricting tapes around the vena caval cannulas released, the superior vena caval cannula clamped and withdrawn, and the inferior vena caval cannula withdrawn into the right atrium, most of the blood flow is maintained through the normal circulation with a smaller portion of the flow passing through the extracorporeal circuit. If the cardiac action is satisfactory the patient is returned completely to his own circulation by clamping the venous and arterial lines from the machine to the patient. While the second row of sutures is placed in the cardiac wound, the apparatus stands by prepared to return the patient to extracorporeal circulation if desired. This is rarely necessary.

Removal of cannulas. After suturing is complete and it is apparent that the heart has resumed its function satisfactorily, decannulation proceeds without delay. The remaining inferior vena caval cannula is removed, and the right atrial appendage is doubly ligated with heavy silk.

The ligatures securing the arterial cannula in position in the subclavian artery are cut and as the cannula is removed a curved hemostat is placed across this artery near the aorta to facilitate ligation of the artery.

The pericardium is left completely open. The thorax is closed, steel wire being used in the transected sternum, and interrupted silk sutures being placed in the intercostal muscles without rib-encircling sutures. The muscles are closed in layers. Two drainage catheters are left in each side of the thorax.

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UNILATERAL CLEFT LIP REPAIR

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IN THEIR OUTSTANDING CONTRIBUTION to cleft lip repair in 1930, Blair and Brown stated, "The logic of the Mirault plan is that a flap is taken from the upper part of the lip where there is excess tissue and implanted in the lower border where tissue is most needed."

In order to take even further advantage of the opportunities afforded by this basic concept, we decided to preserve more tissue on the lateral side of the cleft and introduce it into a notch created medially by dropping the cleft side of the Cupid's bow to its normal position. The incisions are limited, for the most part, to the cleft side of the midline in order to avoid shifting the Cupid's bow from the midpoint of the lip and distorting the remaining philtrum. By introducing tissue in this manner into the lower third of the lip, a more normal pout is obtained, notching of the lip is prevented, and tension on the suture line is reduced. In essence, the Cupid's bow on the cleft side of the midline is dropped to a normal position and the V-shaped defect so created is filled with a flap of the proper dimensions taken from the upper lateral side of the cleft, so as to utilize tissue which might be sacrificed in other procedures. In this manner all possible useful tissue is incorporated to avoid the undesirable effects and appearance of a tight lip. The operation is not carried out until the age of 3 months in order to reduce the margin of error in the apposition of tissues, to permit endotracheal anesthesia with safety, and to take advantage of the ossification of the midfacial bones which gives strength to the dental arch to resist the collapsing force of the repaired lip when accompanied by complete cleft palate, as pointed out previously (2).

From the Cleft Lip and Cleft Palate Center, Medical College Hospital and Department of Surgery (Plastic Surgery), Medical College of South Carolina. Supported by a grant from the National Institutes of Health, D-197 (R).

The procedure is illustrated in Figure 1 and consists of the following steps:

1. *ab* is a line drawn from the apex of the Cupid's bow on the noncleft side to the base of the columella on that side.

2. $a'b'$ is a line drawn from the apex of the Cupid's bow on the cleft side (equidistant from the midline with that of the noncleft side) to the base of the columella on that side.

3. *ab* less $a'b'$ equals x, the distance that the apex of the Cupid's bow must be dropped on the cleft side and equal to the base of the V-flap.

4. Points are marked on either side of the cleft in the floor of the cleft nostril (the medial one on a plane with the base of the columella) so that when approximated, the two nostrils will be similar. The point on the lateral side of the nostril floor is marked b''.

5. Where the vermilion begins to narrow on the lateral side of the cleft, the distance x is measured at a right angle from the mucocutaneous line and point a'' is marked (provisionally).

6. From point b'' a line of length equal to $a'b'$ is dropped to meet the lateral extent of distance

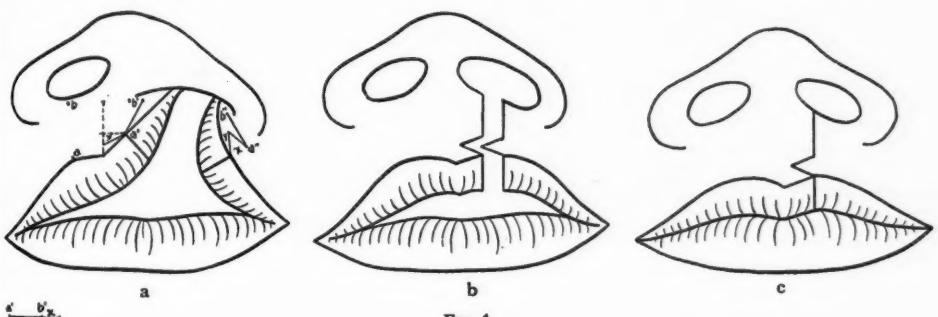
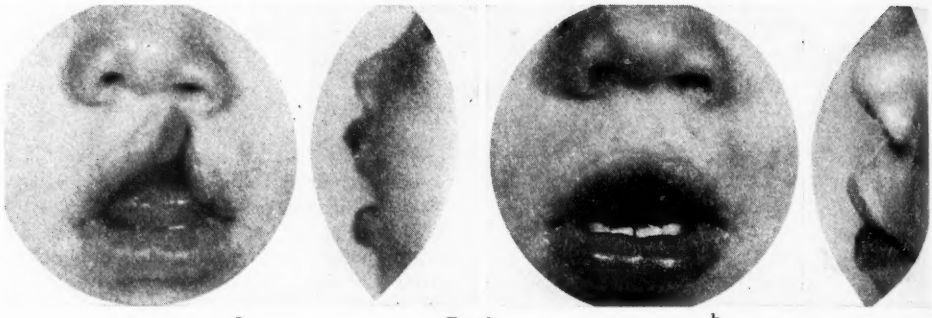
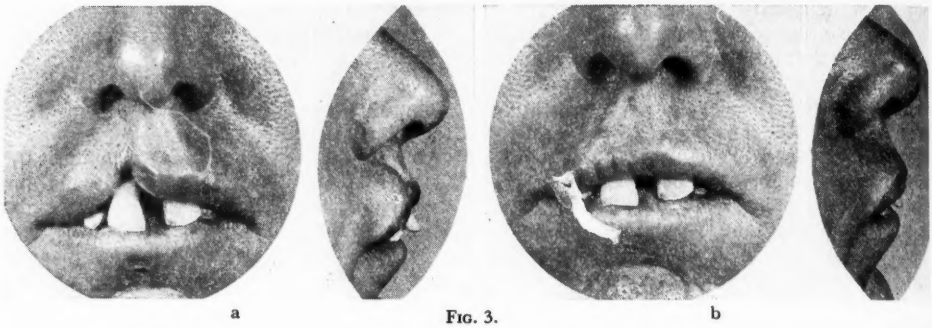


FIG. 1.



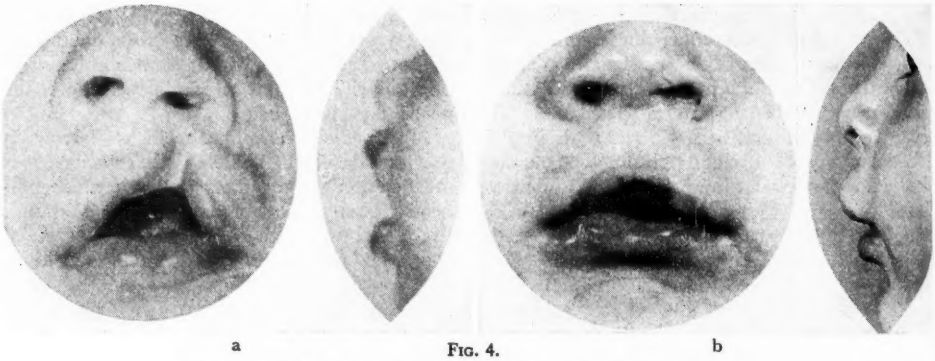
a b

FIG. 2.



a b

FIG. 3.



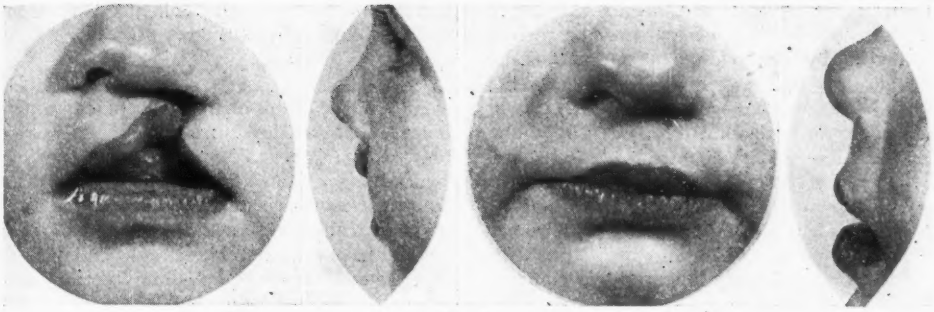
a b

FIG. 4.

FIG. 2. a, Cleft lip incomplete unilateral; b, 15 months postoperative.
FIG. 3. a, Cleft lip incomplete unilateral; b, 4 months postoperative.
FIG. 4. a, Cleft lip incomplete unilateral; b, 2 months postoperative.

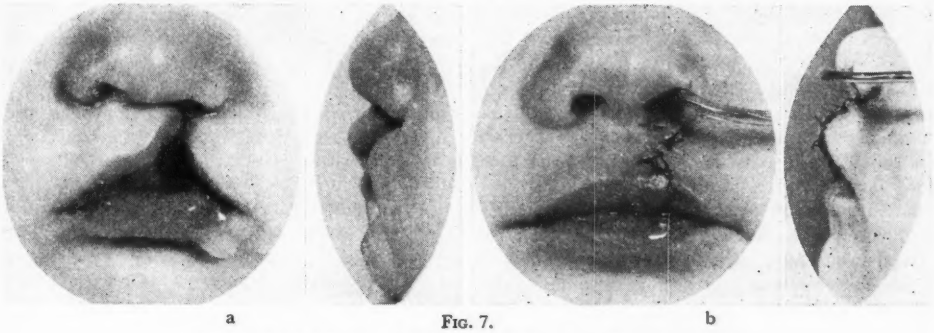
x at a''. If length $a'b'$ fails to extend to a'' that point is raised superiorly. In extreme cases a V-wedge is removed just beneath point b'' to avoid rotating the V-flap off the lip. On the other hand, if length $a'b'$ extends beyond a'', this point can be placed more inferiorly.

7. A line is dropped from the midpoint of the base of the columella to the midpoint of the Cupid's bow. This line is then crossed by a horizontal line passing through the lateral apex of the Cupid's bow at a'. Half way from the midpoint of the Cupid's bow to the cross point of these two lines a point is marked. This point is connected with the apex of the Cupid's bow at



a FIG. 5. b

a FIG. 6. b



a FIG. 7. b

FIG. 5. a, Cleft lip complete unilateral; b, 14 months postoperative.
FIG. 6. a, Cleft lip complete unilateral; b, 7 months postoperative.
FIG. 7. a, Cleft lip complete unilateral; b, 4 days postoperative.

a' and in turn with the point on the medial floor of the nostril to form the line of incision on the medial side of the cleft.

8. The inferior lap of the medial incision is labeled y and this length is used to form either side of an isosceles triangle on base x.

9. Incisions are carried through the full thickness of the lip along these lines located medially and laterally and the lateral V-shaped tongue is introduced into the medial groove, after undermining of the soft tissues and appropriate attention to the nasal deformity.

In the more severe defects a much longer isosceles or even a right triangle of tissue from the

upper lateral lip may be utilized. This larger flap provides more tissue and may be carried beyond the midline to lower the midpoint of the Cupid's bow if necessary. In such cases the medial incision commencing at point a' will approach the horizontal depending upon the configuration of the V-flap.

The final result of lip repair is brought about not only by the apposition of tissue in three dimensions, but also by the interplay of forces such as lip tension, which may be of varied intensity along the suture line, and scar contracture especially along both sides of the triangular flap. An attempt is made in the accompanying line drawing (Fig. 1) to illustrate how the original measurements and lines of incision are affected by these forces, as they come into play.

In Figures 2 to 7, preoperative and postoperative anterior views and profiles are presented to illustrate the application of this method. In Figure 7 the sutures help to accentuate the line of closure.

The reconstruction of the Cupid's bow is complicated by the fact that the normal curvature of the vermilion-cutaneous line is usually absent on the cleft side of the midline. As a result, perfect matching of the two sides of the bow is rarely obtained initially. As can be seen in the postoperative views the apex of the bow on the cleft side usually is lower than that of the noncleft side. In addition, the exact approximation of the vermilion-cutaneous junction is a little more difficult with angled incisions, giving rise to occasional small irregularities. These defects can be readily corrected at a later date, however, by the removal of a narrow crescent of skin at the vermilion-cutaneous border. Such irregularities may accompany any method of repair, but, if confined entirely to one side, their correction is much simpler. Perhaps modifications in technique such as the substitution of a concave curved line for the inferior limb of the triangular flap or the routine projection of the flap across the midline will prove helpful in giving more symmetry to the Cupid's bow.

SUMMARY

After a trial of this method of repair in alternate cases at the Cleft Lip and Cleft Palate Center, Medical College of South Carolina, our results were seen to be sufficiently improved to warrant its exclusive use. In comparison with the previous techniques used, our results with this method have proved to be more dependable, in that the contour of the lip is more normal, the suture line finer, and the Cupid's bow less likely to be displaced. Tissue which would be discarded in other procedures is rotated into the lower aspect of the lip to give a more graduated fullness or pout rather than an exaggerated one in the lower third only. With the utilization of more tissue the lip is approximated with less tension, resulting in a finer suture line. The medial incision, which opens as a groove to receive the tongue created on the lateral side of the cleft, allows the elements of the Cupid's bow to be restored to their normal inferior position. Thus the lateral displacement which accompanies a more vertical incision is avoided and a greater certainty of obtaining symmetry of the lip is provided. In the case illustrations an attempt was made to focus attention on the pertinent anatomy only. The defects in each case become more obvious thereby and their careful study should lead to further improvement. We have as yet not obtained a perfect lip repair but have found that with this method our approach to a normal lip is a little closer.

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Reviews of New Books

THE SECOND VOLUME of Lorenz Böhler's *The Treatment of Fractures*[1] is uniform with Volume I which was recently reviewed. The translation has been made entirely by Russe and Bjornsen.

This volume deals with dislocations and gunshot wounds of the hip joint, fractures of the femoral neck and shaft, including the treatment of pathologic fractures, nonunion, and extension contracture of the knee joint. There is also a section devoted to separation of the proximal femoral epiphysis. The style is similar to that of Volume I, with exhaustive summaries at the end of each section. With the exception of trochanteric fractures, Böhler cannot be accused of incompleteness, nor does he deal cursorily with any side of the subject. The summaries which appear under the heading "Questions We Should Ask Ourselves to Avoid Failures" reach the imposing total of 96 points in relationship to fractures of the femoral neck.

With regard to traumatic dislocations of the hip, the author distinguishes between those injuries due to leverage and those due to thrust. As many patients cannot give an accurate account of the mechanism of their injury, such a division would seem to be arbitrary. The results studied are from 79 recent patients, 43 with a pure dislocation and 28 associated with a fracture of the acetabular ring. In pure dislocations following reduction no postoperative fixation is used, and exercises are started after 2 or 3 days, walking after from 3 to 10 days; both, only if no pain is caused. Böhler claims never to have seen ischemic necrosis of the femoral head after such an injury. His only recorded case of necrosis occurred in a 17 year old boy who, on account of other injuries, had to remain in bed for 10 weeks. In dislocations associated with a fracture of the acetabulum, a manual reduction is performed, and if the joint is stable, the same routine is followed as for pure dislocations. If the bony acetabular fragment is larger, open reduction and internal fixation may be necessary. This is followed by skeletal traction for 12 weeks.

The material on central dislocation of the hip is divided into 3 groups, according to the presence or absence of displacement of the acetabulum in relation to the pelvis as a whole. Skeletal traction through the femur is used to reduce and hold the limb for from 12 to 14 weeks. In some cases, lateral traction is achieved by placing a sling around the upper thigh.

Displaced adduction fractures of the neck of the femur are treated by reduction using skeletal traction followed by tri-fin nailing if the patient is suitable for operation. Treatment by traction alone is discussed at length as is the use of the Whitman plaster. One must ask why, for it is doubtful if anyone at the present time would attempt to treat this fracture in either of these ways. A detailed account of the nailing operation is given; exact reduction is correctly insisted upon and exact placing of the nail also stressed, though one cannot help believing that if a nail is inserted with all the exactness on which Professor Böhler insists is necessary, and one adheres to all details of his nailing technique, the operation must, of necessity, take a very long time. Primary replacement arthroplasty is not advocated, except in patients in whom an exact reduction cannot be obtained, and in Böhler's hands this has only occurred twice in 800 cases. The postoperative routine permits early weightbearing, provided it causes no pain. The published figures show just over 50 per cent of satisfactory results. Böhler briefly mentions Bado's method of internal fixation by fibular graft, followed by immobilization for 3 months in a full hip spica, and says that Bado claims 79 per cent good results by this method, which is undoubtedly a higher proportion than has hitherto been published. As to the cause of complications after operation, Böhler blames any departure from his strict operative routine, but admits that damage to the blood supply of the capital fragment at the time of the accident is probably the most important. For the treatment of nonunion, open subtrochanteric wedge osteotomy and internal fixation by nail plate are advocated. Many patients have also been treated by fixation with the 3 flange nail alone, and 87 per cent of bone union claimed by this method. When avascular necrosis develops, arthroplasty or arthrodesis is employed, but again no detailed discussion is given as to the choice of treatment at this stage.

Separation of the upper femoral epiphysis is treated along conventional lines, recent early slipping being treated by internal fixation or by Whitman plaster. Recent severe slips are reduced by manipulation then fixed by pins or nail; reduction by traction in this group is condemned. Late cases with gross deformity are treated by corrective subtrochanteric osteotomy, and osteotomy of the neck of the femur is not advised.

In trochanteric fractures, reduction is achieved by skeletel traction, and this is followed in suitable cases by nail plate fixation. Böhler allows early weight-

[1] THE TREATMENT OF FRACTURES. By Lorenz Böhler, M.D. Vol. II. 435 pages, 941 illustrations. $17.50. New York and London: Grune & Stratton, Inc., 1957.

bearing in all nailed cases, and no untoward results are recorded. No mention is made of nonunion or its treatment.

Fractures of the femoral shaft are treated by skeletal traction and the Böhler-Braun splint. The traction pin, initially always driven through the upper tibia, is transferred to the lower femur after 4 weeks. This is said to avoid damage to the knee joint. Böhler issues a stern warning against the use of excessive traction. Operative fixation, and especially the use of metal plates, is condemned, but in recent years open reduction and Kuntscher nailing has been used in suitable cases, and is now regarded as the method of choice in fractures which can be stabilized by this method. A wire loop is always inserted as an insurance against rotation. Supracondylar fractures are treated by traction and with the Braun frame, but operative fixation is sometimes employed and wire transfixion of the lower fragment with subsequent plaster spica immobilization is also described.

Leg equalization in the Böhler clinic is always performed by shortening the sound femur and fixing it with a Kuntscher nail, and the poor results of lengthening the short leg are commented upon.

In summary, this volume gives a very full and detailed account of the surgery of the hip and femur following injury and records the complications to be encountered. Böhler's results with the trifin nail approximate to those from other sources, and are obviously still a matter for concern. By comparison with Volume I, the second volume seems briefer, easier to read, and contains less unrelated material. One would have expected a better guide in the problem of the failed Smith-Petersen nail. Early failure is treated by renailing, but this is obviously as likely to fail, and nonunion is again usually treated by renailing with a proportion of successful cures. The other procedures which have been used include all recognized alternatives, with no clear guide as to which method has been most often performed and no statistical details available to make comparison as to which procedure could be regarded as the most satisfactory method of dealing with this complex problem.

—*Harold Bolton.*

A WELL WRITTEN AND ILLUSTRATED collection of papers edited by the Instituto Ortopedico Toscano of Florence, Italy, is presented in *Archivio "Putti" di Chirurgia Degli Organi di Movimento*[2]. Most of the papers deal with problems related to the diagnosis and treatment of bone tumors accompanied by presentation of cases and appended with world literature.

Among the outstanding papers, there is one in which 27 cases of "giant cell sarcoma" are presented with clinical, radiologic, histologic, and follow-up studies. It is also preceded by a historical review of that tumor. One of the reported cases because of its location in the clavicle, the age of the patient, and the gross characteristics is suggestive of an aneurysmal bone tumor; however, the presence of numerous giant cells that usually accompany these lesions probably misled the authors to make the diagnosis of giant cell tumor. In another patient of 16 years of age there is also some doubt as to the diagnosis.

The report of 2 cases of chondromyxomatous tumors is interesting because of its rarity in children and the discussed relationship between these entities. Another outstanding paper presents a classification of bone tumors based on a series of 1,440 cases. In general, the classification agrees with modern concepts in bone disease, but there is a remarkably low incidence of multiple myeloma as compared with its incidence in this country. This is probably explained on the basis of the purely orthopedic material handled by that institution. The relationship between trauma and neoplasm is discussed in another article with the same negative results already reported in other countries.

The interesting hypothesis of the granulomatous origin of osteoid osteoma produced by an unknown organism is accompanied by the presentation of 22 cases with clinical, radiologic, and relatively weak histologic evidences. Most of the cultures were negative.

Thirty-three cases of tuberculous tenosynovitis are reported in another paper with remarks on frequency, localization, pathogenesis, occupational relationship, and treatment.

Worth mentioning are the clinopathologic studies of glomus tumor, parosteal angioma and lipoma, treatment of chronic rheumatic tenosynovitis, and the article in which a new bed for treatment of scoliosis is presented. All of them are accompanied with the presentation of cases. Other papers are devoted to the "Josephinum" (pathologic and anatomic Museum in Vienna) and biographies of outstanding pioneer orthopedic surgeons from Italy and New York.

The book deserves commendation for the excellent work done by the members of the Instituto Ortopedico Toscano.

—*Hector Marquez.*

THE VOLUME entitled *Pediatric Cardiology*[3] by Alexander Nadas of Harvard Medical School and the Children's Medical Center, Boston, is described in the preface as "—a handbook for the pediatrician, the general physician, and the medical student." It will also interest many surgeons and it is certain to become a popular book for there is no comparable up-to-date monograph in this dynamic field.

The book has 4 parts: The Tools of Diagnosis, Acquired Heart Disease, Congenital Heart Disease, and Anesthesia for Children with Heart Disease. As would be expected, the part on congenital heart disease is the longest (268 pages), and the section on anesthesia is the shortest. Except for the fact that this last section appears to be added without good cause, the organization is sound.

The text makes good reading straight through, from beginning to end, yet any particular section is clear in itself. This virtue of sectional independence will permit the student to use the book as a handy reference manual. It is certain to serve this function, yet, as the author points out, he did not intend to write a reference book. The list of bibliographic references, though

[2]ARCHIVIO "PUTTI" DI CHIRURGIA DEGLI ORGANI DI MOVIMENTO. Director, O. Scaglietti. Vol. VII. 470 pages, illustrated. Firenze: Edizioni Scientifiche Dell' Instituto Orthopedico Toscano, 1956.

[3]PEDIATRIC CARDIOLOGY. By Alexander S. Nadas, M.D., F.A.A.P. 587 pages, 343 illustrations. $12.00. Philadelphia and London: W. B. Saunders Co., 1957.

long enough to be helpful to the beginner, is incomplete. The manual is written principally about the author's own experience, and it is not a review of the work of others. Doubtless, this is the best way to cover an active field of medicine in a coherent manner in a book of this size. Nadas has done an admirable job, but each reader interested in the field will inevitably have exceptions to take and suggestions to make.

Though the book is not designed for surgeons, I would like to make a few comments from a surgeon's point of view. The text is behind the times on modern surgical methods. There is almost nothing on open intracardiac techniques, not even adequate references. For one who contemplates repair of cardiac defects, illustrations of the embryologic development of the congenital defects and good pictures of the pathologic anatomy are needed. In most cases there are no such illustrations. This lack was most apparent to me in fields in which I have had some interest, such as atrial septal defects and total anomalous pulmonary venous drainage.

Again, from the surgeon's special point of view, the book has important virtues. The material on the clinical picture of diseases and on differential diagnosis is generally excellent. Any surgeon who plans to do cardiac surgery needs, and often sadly lacks, competence in these vital aspects of heart disease. This book will help him. —*F. John Lewis.*

DOCTOR MOORE puts into a single volume,[4] his extensive studies on hyperostosis cranii, a condition which occurs predominantly in women and which is characterized by roentgenologically demonstrable changes in the skull, obesity, and male type of facial hirsutism. The author uses roentgenograms collected for over 30 years as a starting point and a foundation of his investigation. To these data is added and correlated information largely obtained from hospital and patient records, and from anatomic material at the Washington University Medical Center in St. Louis.

Since all investigations of this condition are handicapped by the lack of pathologic material and since opinions differ as to the nature of the conditon, the author approaches the subject from the standpoint of a detached recorder of observed facts rather than of an advocate. After discussing the syndrome from every aspect, the writer fully subscribes to Henchen's view that the condition is an abnormality of pituitary function. He advances the theory that "hyperostosis and its syndrome are the manifestation of an endogenous intoxication, traceable to the aberrance in some unknown phase of function of reproduction."

Readers interested in this common and poorly understood condition will find the volume valuable. —*F. E. Templeton.*

THE TEXT *Clinical Use of Radioisotopes*[5] by Beierwaltes, Johnson, and Solari is an excellent and compact volume. It should be available to all those interested in this new field of medicine, and also for those who may wish to take advantage of the numerous tests developed in this field.

The 438 pages are filled with information and data necessary to the experienced and beginning isotopologist. A few of the outstanding chapters are: chapters 1 and 14 which deal with preliminaries necessary for establishing an isotope unit. Chapters 2 to 6 deal with the thyroid and special techniques with radioactive iodine. Chapters 7 to 10 deal with phosphorous, gold, and also a group of less used isotopes. Chapters 11, 12, and 13 deal with the biologic effects of radiation, health, physics, and instrumentation.

The appendix has valuable tables and information on sources of radioactive isotopes.

As one can see there is a great deal of medical information in this fine little book. The content is as clear as it is concise. —*J. E. Kearns.*

IT IS EXPLAINED by the publisher, and by J. P. Webster, in the foreword, that *The Principles and Art of Plastic Surgery*[6] by Gillies and Millard is not only a book of plastic surgery but also the autobiography of the senior author. As such, it will be of great interest to all plastic surgeons, and especially to those who have worked, or taken courses, with him.

The book may be of added interest to American plastic surgeons for several reasons. Gillies states that his first inspiration in the work came from a German book, given him by his American dental friend, Bob Roberts, who said, "Why don't you take up this work?" The senior author has chosen an American as coauthor, saying of him—"without (his) faith and vision this book would never have been started: long, lithe, lanky Yankee blessed with a happy pun, a love of plastic surgery, and an unfailing blind belief in his coauthor."

Gillies chose another American, J. P. Webster, to write the foreword, who explains, "In D. Ralph Millard, who came to work with him, Gillies recognized a kindred spirit, another Puck. Perhaps, it was this similarity of personality that caused Gillies to ask Millard to return to help produce this book. It has been a felicitous collaboration, undoubtedly stimulating to both authors." Finally, the senior author chose an American publisher, and gives much credit to Mr. Ted Phillips of Little, Brown and Company.

The junior author, in the preface, states of the book that "the theme throughout is the perpetual Battle of Beauty versus Blood Supply." The senior author a little later, under "Principles," carries on with this theme stating that it is the father and mother of all principles. From the junior author's preface, it is noted that the book—"has been 4 years in the making and covers 40 surgical years." With such a background, and the widely known name of Gillies on this work, there is no question of its success, and it is not the province of a review to try to add to or to detract

[4] HYPEROSTOSIS CRANII. STEWART-MOREL SYNDROME; METABOLIC CRANIOPATHY, MORGAGNI'S SYNDROME; STEWART-MOREL-MOORE SYNDROME (RITVO). LE SYNDROME DE MORGAGNI-MOREL. By Sherwood Moore, M.D. 226 pages, 107 illustrations. $10.50. Springfield, Ill.: Charles C Thomas, 1955.

[5] CLINICAL USE OF RADIOISOTOPES. By William H. Beierwaltes, M.D., Philip C. Johnson, M.D., and Arthur J. Solari, B.S., M.S. (Physics). 438 pages with 126 illustrations. $11.50. Philadelphia, and London: W. B. Saunders Co., 1957.

[6] THE PRINCIPLES AND ART OF PLASTIC SURGERY. By Sir Harold Gillies, C.B.E., F.R.C.S., and D. Ralph Millard, Jr., M.D. Chapter on Anaesthesia by Ivan Magill, C.V.O., F.F.A.R.C.S. With a foreword by Jerome Pierce Webster, M.D. Vols. I and II. 317 and 332 pages, illustrated. $35.00. Boston and Toronto: Little, Brown & Co., 1957.

from such an autobiographic text. Rather, this reviewer would defend the book, in questions of text, on the basis of the huge task involved and of the over-all result produced.

Some questions have arisen regarding the innumerable illustrations, as many as 38 on one page, and of their size, some no larger than a postage stamp. Some of the photographs and diagrams could be clearer. The complete lack of legends for each figure except in the atlas-style accompanying text has been criticized, as has some of the arrangement of material, for example the inclusion of cancer and radiation burns under the heading "Mostly Congenital."

Occasionally the usage of words, such as harelip for cleft lip and of chordee (which denotes veneral disease) for curvature in hypospadias, might be questioned, as might the advocating of the use of beef cartilage. An answer to all of these queries is that this is a personal autobiographic work from which even the most erudite can learn.

If one does not quite understand some of the photos or drawings, there are plenty of others; in fact, there are so many a photograph-meter would be needed to count them. As for usage of words, valuable material is of more importance than an exact establishment of every source.

No references to the literature are given, not even any of the authors', but this, also, is an autobiographic choice and leaves a hundred or so pages for more of the authors' work.

The authors' statements about private practice are still again of autobiographic choice—"a great percentage of private practice is beauty surgery. It is here that perfection is a necessity. Reconstructive surgery is an attempt to return to normal; cosmetic surgery is an attempt to surpass the normal. No man is a plastic surgeon unless he becomes adept at both. Many never do and are a menace." Possibly these ideas may be influenced by life in the Emergency Medical Service of World War II and of socialized medicine since then, but again something may be learned for the advent of socialization of all effort.

In the epilogue, concerning the junior author, is found the statement, that "In the United States Navy in World War II he continued in plastic surgery . . . In 1948, he went to England to study under Sir Harold Gillies . . . returned to America . . . was entrusted with the organization of the Plastic Surgery service for the Baylor Medical School, Houston, Texas." He was invited by Gillies in 1952 "to be coauthor." After completion of the manuscript, he rejoined the United States Navy, worked with the Marines and "because of his original work in Korea, he was invited to give a paper at the first International Congress of Plastic Surgeons."

There is full documentation of the senior author's career and in the epilogue is included the comment, "He devised the tube pedicle flap, the onlay eyelid graft, the palate push-back . . . but most important, he has organized and taught the fundamental principles of present day plastic surgery."

—*James Barrett Brown.*

JONATHAN MEAKINS has been producing a textbook of medicine regularly for over 20 years, and the sixth edition of *The Practice of Medicine*[7] is his best publication. In the preface he recognizes the fact that there is an increasing tendency for professors of medicine to be specialists in some branch of this profession and that this is good for the graduate student. However, where the undergraduate and the practitioner of medicine are concerned the most helpful teacher of medicine is the one who can fill in the odds and ends of the diversified lesions and syndromes. Such a man must be able to discuss fundamental concepts at the bedside and inspire in the student or practitioner a grasp of the art and science of medicine. Also the task of healing the physical disabilities and of recognizing the emotional factors that predispose to and result from such complex integrations must fall to him.

The editorial staff of this edition includes 24 associate editors and 86 contributors, each contributing a discussion concerning his own particular realm. These men have constant contact with humanity, both in the hospital and the out-patient department. They possess a broad understanding of the unity of medicine and ably co-ordinate the anatomic, physiologic, emotional, and environmental whole. They are inspired through contact with the younger generation, and in the text "act as a fly-wheel to keep the practice of medicine at an even speed when the enthusiasms and narrow outlook in special branches are apt to ignore the broad principles of medicine."

The text considers infectious disease from the standpoint of the bacterium and other pathogens rather than the specific disease as in earlier editions. The section on chemotherapy and antibiotics has been expanded to deal with all aspects of the subject including indications, specific action, selection, complications, combinations, and misuse. Similarly other diseases are discussed with a final section on psychosomatic medicine, "designed to knit the general concepts of this branch of medicine into an integrated whole." References have been kept to a minimum but are quite adequate.

In general the editor and his associates have presented us with a modern textbook of medicine which appears adequate for the medical student and practitioner of medicine. They are to be congratulated for producing a concise, easy to read, clearly printed text with numerous illustrations and charts which, in themselves, are helpful. —*George C. Turnbull.*

THE BOOK entitled *1957 Medical Progress*[8] is a review of medical advances during 1956. It is edited by Morris Fishbein, M.D., and there are 29 contributors who were selected because of their knowledge of current literature and their ability to present briefly new concepts and conclusions.

It is essentially a year book which covers all fields of medicine and therefore is of chief interest to students and those interested in the general practice of medicine. The individual contributors, some of whom

[7] THE PRACTICE OF MEDICINE. Edited by Jonathan Campbell Meakins, C.B.E., M.D., LL.D. D.Sc. 6th ed. 1916 pages, 318 illustrations, with 4 of the illustrations in color. $16.00. St. Louis: The C. V. Mosby Co., 1956.

[8] 1957 MEDICAL PROGRESS; A REVIEW OF MEDICAL ADVANCES DURING 1956. Edited by Morris Fishbein, M.D. 367 pages, not illustrated. $6.00. New York, Toronto, and London: The Blakiston Division, McGraw-Hill Book Co., Inc., 1957.

have contributed to previous volumes, discuss those subjects which are of special interest to them. This results in some natural overlapping which has the advantage of presenting different points of view. At the end of each section there is a list of references which increases the usefulness of this volume.

—*R. T. Bothe.*

THE EXCELLENT TEXT entitled *Hemorrhagic Diseases*[9] represents Dr. Quick's third monograph on coagulation and its disorders. He has retained in the present volume much of the interesting historical detail presented in his previous two books, and he has extensively revised and brought up to date the material pertinent to the clinical and laboratory aspects of hemorrhagic diseases.

The text is well organized. Each chapter of the clinical part, dealing with a specific disorder or group of disorders, is sufficient unto itself. Thus the reader is permitted to review (history, diagnosis, treatment) a given disorder without reference to other portions of the text. However, such a style does lead to repetition. The laboratory methods section outlines 25 specific diagnostic procedures in detail.

The clinical descriptions of the various disease states are good, and the presentations of therapy are most complete. The discussion of the many agents in use for prolongation of clotting is timely. The text suffers here and there from the animadversions of the author, and some of his concepts, such as the presence of an inactive state of prothrombin, prothrombinogen, are not accepted by all workers in the field of coagulation.

The book is to be recommended to the internist as a source of helpful information in those vexing diagnostic problems of hemostasis, and to the the hematologist interested in coagulation as a clear exposition of Dr. Quick's views in the ever changing field of coagulation disorders. —*Walter A. Rambach.*

THE SMALL BOOK entitled *Der hohe Gradstand*[10] by Möbius and Hilmerth is devoted to the unusual obstetric condition in which the baby's sagittal suture remains in or above the pelvic inlet in an anteroposterior diameter or nearly so, for a long time at the beginning of labor. This monograph is essentially a long article on the subject, hence it does not lend itself to a review. During the last 20 years 194 such cases have been observed at the Leipzig Women's Clinic. Since these cases occurred among 66,796 deliveries the incidence of this condition is 0.3 per cent in 3 cases per 1,000. The frequency of occiput anterior was 60.3 per cent and of occiput posterior 39.7 per cent. Only 38.1 per cent of the patients were multiparas and only 54 patients had normal pelves. Flat pelves were observed in 53 cases but wide pelves were present in 51. Obviously the diagnosis of a high anteroposterior head is made much more frequently by x-ray than by clinical examination. Delivery was spontaneous in only 26.3 per cent of the cases. The authors emphasize that cesarean section is the most satisfactory method of treatment. The maternal mortality was 1.5 per cent and the fetal death rate 8 per cent.

At the end of the monograph is a list of references, practically all of which are German.

—*J. P. Greenhill.*

MOST MODERN TEXTBOOKS OF PHYSIOLOGY contain upwards of 1,000 pages. One is startled, therefore, in confronting a text[11] of less than half the usual size, to note that it purports to be a reasonably comprehensive treatise for students of the medical sciences. One is still further startled, on reading the text, to discover that the author has accomplished this objective in a truly magnificent manner. To quote from the preface: "The brevity of the book is achieved in considerable degree by omitting most of the background material which is commonly included in the larger textbooks of physiology but which has been covered by students who have already taken courses in anatomy and biochemistry. Thus, anatomy is not reviewed and biochemical topics are reduced virtually to synopses . . . . Secondly, the brevity of this book is related to the fact that no systematic coverage of clinical physiology is attempted."

It should be emphasized that brevity is not achieved by resort to outline forms of presentation or by sacrifice of explanatory and illustrative material, both of which methods are not infrequently used for such a purpose. The writing is lucid and interesting, there are some 180 illustrations which are pertinent and instructive, and the printing and physical make-up of the book are excellent. The index is satisfactory and the bibliographic citations, although rather limited as would be expected in a treatise of this dimension, are very well chosen. Since this is a single author production it is to be expected that some areas of the subject are treated somwhat more extensively than others, but the author has done a remarkable job with an extraordinarily difficult task. —*Carl A. Dragstedt.*

THE FINE BOOK entitled "*Controlled Hypotension*" *in Anesthesia and Surgery*[12] contains much of specific interest to anesthesiologists. It brings together information both past and present, laboratory and clinical, on the intentional production of hypotension to achieve a relatively bloodless operative site. The first part of the book discusses the factors which produce excessive bleeding during surgery, and which maintain arterial blood pressure; and the physiologic basis of the techniques for inducing hypotension. The author then describes in detail the various techniques of controlled hypotension with particular reference to their relative advantages and disadvantages. The latter part of the book treats with the physiologic derangements inherent in controlled hypotension and the occurrences of fatal and nonfatal complications, information collected from questionnaires sent to the members of the Association of Anesthetists of Great Britain and Ireland, and to Diplomates of the American Board of Anesthesiology, and based on 27,930 cases of con-

[9] HEMORRHAGIC DISEASES. By Armand J. Quick, Ph.D., M.D. 451 pages, 37 illustrations. $9.50. Philadelphia: Lea & Febiger, 1957.

[10] DER HOHE GRADSTAND. By Prof. Dr. Med. W. Möbius and Dr. Med. Harold Hilmerth. 71 pages, 21 illustrations. DM 10.90. Leipzig: Georg Thieme, 1957.

[11] FUNDAMENTALS OF HUMAN PHYSIOLOGY FOR STUDENTS IN THE MEDICAL SCIENCES. By W. B. Youmans, Ph.D., M.D. 567 pages, illustrated. $8.50. Chicago: Year Book Publishers, Inc., 1957.

[12] "CONTROLLED HYPOTENSION" IN ANESTHESIA AND SURGERY. By David M. Little, Jr., M.D. 159 pages, 14 illustrations. $4.50. Springfield, Ill.: Charles C Thomas, 1956.

trolled hypotension. The contraindications are then defined, and a set of indications suggested. An extensive bibliography of over 500 references is included, embracing all the works referred to in the text.

The printing, paper binding, and general format of this book are excellent. There is a very adequate index.

This manual is recommended to the anesthesiologist as a comprehensive study of the present day knowledge of controlled hypotension.—*Mary Karp.*

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

OPERATIVE OBSTETRICS. By R. Gordon Douglas and William B. Stromme. 735 pages, illustrated. New York: Appleton-Century-Crofts, Inc., 1957.

NOUVELLE PRATIQUE CHIRURGICALE ILLUSTRÉE. Jean Quenu, directeur. Fascicule X. By S. Dupret, R. de Boisgontier, F. de Perrois, and P. Rivallain. 295 pages, 252 illustrations. 3,200 fr. Paris: G. Doin & Cie, 1957.

LES MÉNINGIOMES; ÉTUDE CLINIQUE ET CHIRURGICALE. By J. Guillaume, R. Billet, J.-P. Caron, and D. Cuccia. 173 pages, illustrated. Paris: Presses Universitaires de France, 1957.

LES ACCIDENTS CIRCULATOIRES DU CERVEAU; TRAITEMENT CHIRURGICAL DE L'HÉMORRAGIE ET DE L'ISCHÉMIE. By J. Guillaume, G. Mazars, R. Roge, and A. Pansini. 141 pages, illustrated. Paris: Presses Universitaires de France, 1957.

THE STORY OF PEPTIC ULCER. By Richard D. Tonkin, M.D. 71 pages, illustrated. $2.25. Philadelphia: W. B. Saunders, 1957.

INTRODUCTION TO ANESTHESIA; THE PRINCIPLES OF SAFE PRACTICE. By Robert Dripps, M.D., James Eckenhoff, M.D. and Leroy Vandam, M.D. 254 pages, illustrated. $4.75. Philadelphia: W. B. Saunders, 1957.

TUMOR SURGERY OF THE HEAD AND NECK. By Dr. Robert S. Pollack. 101 pages, illustrated. $5.00. Philadelphia: Lea & Febiger, 1957.

GERICHTLICHE GEBURTSHILFE. By Prof. Dr. H. Naujoks. 247 pages, not illustrated. $6.40. Stuttgart: George Thieme , 1957.

FORTSCHRITTE DER GEBURTSHILFE UND GYNAEKOLOGIE. By A. Reist. 103 pages, illustrated. S.Fr. 15.60. Basel, Switzerland: S. Karger A. G., 1957.

A SYSTEM OF OPHTHALMIC ILLUSTRATION. By Peter Hansell, M.R.C.S., F.R.P.S., F.B.P.A. 114 pages, illustrated. $5.75. Springfield: Charles C Thomas, 1956.

BODY WATER IN MAN: THE ACQUISITION AND MAINTENANCE OF THE BODY FLUIDS. By Maurice B. Strauss, M.D. 286 pages, 31 illustrations. $7.00. Boston: Little, Brown & Co., 1957.

HOFTEALLOPLASTIK SOM BEHANDLING OVERFOR EGNEDE TILFAELDE AF FRACTURA COLLI FEMORIS OG SPECIELT FØLGETILSTANDE HEREFTER. By R. Movin. 275 pages, illustrated. d. kr. 25,00. København: Ejnar Munksgaard, 1957.

THE CLOSED TREATMENT OF COMMON FRACTURES. By John Charnley, B.Sc., M.D., F.R.C.S. 2nd ed. 260 pages, illustrated. Baltimore: Williams & Wilkins Co., 1957.

BONE TUMORS; GENERAL ASPECTS AND AN ANALYSIS OF 2,276 CASES. By David C. Dahlin, M.D. 224 pages, illustrated. $11.50. Springfield, Ill.: Charles C Thomas, 1957.

SIR GEORGE BUCKSTON BROWNE. By Jessie Dobson, B.A., M.Sc., and Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., D.Sc., F.R.C.S., F.R.A.C.S., F.A.C.S. 143 pages, illustrated. $6.00. Edinburgh and London: E. & S. Livingstone Ltd.; Baltimore: Williams & Wilkins Co., 1957.

STEDMAN'S MEDICAL DICTIONARY. 19th rev. ed. Edited by Norman Burke Taylor, V.C., M.D., F.R.S.C., F.R.C.S., and Lieut. Col. Allen Ellsworth Taylor. 1656 pages, illustrated. $12.50. Baltimore: Williams & Wilkins Co., 1957.

MANAGEMENT OF COMPLICATIONS IN EYE SURGERY; AVOIDANCE OF PITFALLS AND TREATMENT OF DIFFICULT SITUATIONS IN OPHTHALMOLOGIC OPERATIONS. Edited by R. M. Fasanella, M.D. 422 pages, illustrated. $16.00. Philadelphia and London: W. B. Saunders Co., 1957.

ORTHOPEDICS FOR THE GENERAL PRACTITIONER. By William E. Kenney, M.D., and Carroll B. Larson, M.D., F.A.C.S. 413 pages, 180 illustrations. $11.50. St. Louis: C. V. Mosby, 1957.

PEDIATRIC ROENTGENOLOGY. By Dr. M. A. Lassrich, Prof. Dr. R. Prévôt, and Prof. Dr. K. H. Schäfer. Edited by Prof. Dr. K. H. Schäfer. Translation from German by James T. Case, M.D. 333 pages, 700 illustrations. $28.00. New York and London: Grune & Stratton, Inc., 1957.

TRANSACTIONS OF THE SOUTHERN SURGICAL ASSOCIATION. Vol. 68. Edited by George G. Finney, M.D. 443 pages, illustrated. Philadelphia and Montreal: J. B. Lippincott Co., 1957.

ANATOMIES OF PAIN. By K. D. Keele, M.D., F.R.C.P. 206 pages, illustrated. $5.50. Springfield: Charles C Thomas, 1957.

ROENTGEN DIAGNOSIS OF ABDOMINAL TUMORS IN CHILDHOOD. By Charles M. Nice, Jr., M.D., Ph.D., Alexander R. Margulis, M.D., and Leo G. Rigler, M.D. 75 pages, illustrated. $4.00. Springfield, Ill.: Charles C Thomas, 1957.

SELECTED WRITINGS OF WALTER E. DANDY. Compiled by Charles E. Troland, M.D., and Frank J. Otenasek, M.D. 789 pages, illustrated. Springfield, Ill.: Charles C Thomas, 1957.

OSTETRICIA E GINECOLOGIA; AD USO DEGLI STUDENTI E DEI MEDICI PRATICI. Vols. I and II. By Espedito Moracci. 1333 pages, 595 illustrations. Napoli: Casa Editrice Idelson di E. Gnocchi e F., 1957.

TRANSACTIONS OF THE PACIFIC COAST OBSTETRICAL AND GYNECOLOGICAL SOCIETY. Vol. XXIV. 202 pages, illustrated. Portland: Western Journal of Surgery Publishing Co., 1957.